EXHIBIT A

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

CHARU DESAI, Plaintiff, v. UMASS MEMORIAL MEDICAL CENTER, INC.; UMASS MEMORIAL MEDICAL GROUP; UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, UMASS MEMORIAL MARLBOROUGH HOSPITAL, MAX ROSEN, M.D., DARREN BRENNAN, M.D., STEPHEN TOSI, M.D., AND KARIN DILL, M.D., Defendants.	CIVIL ACTION NO.: **4:19-CV-10520-DHH**

PLAINTIFF CHARU DESAI'S EXPERT WITNESS DISCLOSURE

The Plaintiff, Charu Desai, M.D., by and through her attorneys, discloses the witness listed below may be called at trial to offer expert testimony.

I. *Disclosure – Michael Morrison, Ph.D.*

Plaintiff expects to call Michael Morrison, Ph.D., to offer expert opinion testimony. Dr. Morrison is a tenured Assistant Professor of Economics at Edinboro University of Pennsylvania and the Assistant Department Chair of the Department of Business and Economics. He earned a Bachelor of Sciences in Economics in 2004 from Montana State University in Bozeman, Montana. Dr. Morrison then earned a Master's degree in Economics in 2012, at the University of New Mexico, in Albuquerque, New Mexico. He earned his Ph.D. in economics in 2013, also at the University of New Mexico. Dr. Morrison has substantial teaching experience, having

taught economics for over ten years. Dr. Morrison has also published several papers, presented at conferences, and given numerous lectures in the field of economics.

Dr. Morrison's report includes a complete statement of all opinions to be expressed and the basis and reasons therefore, the information considered in forming the opinions, and any exhibits to be used as a summary of or support for the opinions; a copy of his curriculum vitae, which details Dr. Morrison's qualifications; a listing of all publications Dr. Morrison authored within the preceding ten (10) years; and a listing of other cases Dr. Morrison has testified at trial or by deposition in the preceding four (4) years. In this case, Dr. Morrison is being compensated $1,750 for his study and a rate of $350.00 for any additional testimony.

Plaintiff expects that Dr. Morrison will offer testimony on issues related to lost economic benefits, including salary and retirement benefits, due to her employment discrimination.

More specifically, Dr. Morrison will testify concerning the below:

- The present value of Plaintiff's lost past and future earnings as a result of her termination; and
- The present value of Plaintiff's reduced quality of life associated with her major depressive disorder, which resulted from Dr. Desai's termination.

II. *Reservation of the Right to Rebut and Comment*

Plaintiff reserves the right to supplement and amend this disclosure as discovery is ongoing. Plaintiff reserves the right to have her expert critique, comment upon and rebut the testimony and opinions of the Defendant's experts, if any. Plaintiff further reserves the right to call as an expert witness any person disclosed by the Defendant as an expert witness. Plaintiff reserves the right to elicit from such witness testimony on any of the issues in this case without specifically adopting the testimony and opinions of the Defendant or the Defendant's experts.

Respectfully Submitted,

CHARU DESAI,
By her attorneys,

/s/ Patricia A. Washienko
Patricia A. Washienko, BBO# 641615
pwashienko@fwlawboston.com
Brendan T. Sweeney, BBO # 703992
bsweeney@fwlawboston.com
FREIBERGER & WASHIENKO, LLC
211 Congress Street, Suite 720
Boston, MA 02110
p: 617.723.0008 f: 617.723.0009

Dated: August 1, 2021

CERTIFICATE OF SERVICE

I, Brendan T. Sweeney, hereby certify that a true and accurate copy of the foregoing document was served upon attorneys for the Defendants herein, by electronic mail.

/s/ Brendan T. Sweeney
Brendan T. Sweeney

Dated: August 1, 2021

EXHIBIT B

Michael Morrison Ph.D.
Economic consulting

5205 Caprock Dr. NE, Rio Rancho, NM 87144
Tel: 505-231-0041
Mtmichael@gmail.com

Economic Report

To: Patricia A. Washienko, Esq.

From: Michael Morrison Ph.D.

Date: 07/27/2021

Re: *Dr. Desai v. UMass Memorial Health, et al.*

Part I Background

Dr. Desai is a 71 year old (July 6, 1950) woman residing in Worcester, Massachusetts who was a radiologist at the UMass Memorial Health ("Employer"). She was hired 27 years ago (in 1992) as a Radiologist and served as Radiologist until March 17, 2019.

It is my understanding that prior to her termination Dr. Desai was paid $340,000.00 per year in salary as well as receiving an 8% contribution to her 401k plan, life insurance coverage valued at $50,000.00, and Continuing Medical Education expenses valued at $4,000.00 per year. Dr. Desai was employed at UMass Hospital for 27 years and planned to continue her employment for an additional 10 years. On March 17, 2019, Dr. Desai's employment was terminated from UMass Hospital.

Dr. Desai believes she was terminated due to discrimination. As a direct result of Dr. Desai's termination, she was diagnosed with major depressive disorder and has been n the care of psychiatrist and on medication since her diagnosis on May 25, 2020.

Prior to her termination of employment, Dr. Desai learned that a younger co-worker was receiving in addition to their regular compensation 1.5 academic/administrative days per week. On academic/administrative days the co-worker was not required to perform clinical duties. Dr. Desai also is aware that another younger co-worker was paid $10,000 per year more than her since 2016. Dr. Desai contends that this is further evidence of discrimination.

Assignment

I have been retained to form an opinion to a reasonable degree of economic certainty as to the present value of lost earnings and the value of reduced quality of life associated with major depressive disorder resulting from Dr. Desai's termination.

The Basis for Economic Damages

Economic damages related to lost earnings are based on the economic concept of *opportunity cost*. If, as a result of an illegal act, a person is deprived of the opportunity to earn a living, the resulting damages are equal to the cost of restoring the injured person's lost opportunity or providing what would have reasonably been the fruits of exercising it. In this case, it is alleged that Dr. Desai was wrongfully terminated due to discrimination. Her early termination prevented Dr. Desai from continuing to work. Additionally her termination caused her to develop major depressive disorder, which reduced her quality of life; preventing her from fully enjoying her leisure time. The calculation of the value of the reduced quality of life is a 3-part process.

1. Establishing the value of time. This has been done based on the employee's contractual salary as of $340,000.00/year, which represents an agreement between Employer and Dr. Desai about the minimum value of her time. This number is converted to a daily rate, assuming a 52-week contract. This figure is then applied to a full 24-hour day. This number represents what Dr. Desai is willing to accept for 24 hours of her time. This isn't related to Dr. Desai's employability, instead it is Dr. Desai's value of her leisure time.
2. Establishing the reduction in quality of life. This is a measure of how much the major depressive disorder has reduced her quality of life. This is essentially the same concept as quality-of-life adjusted life expectancy. Through a survey of relevant academic research (from refereed sources), several "suffering multipliers" have been gathered. A corresponding value of reduced quality of life has been calculated for each multiplier and is reported in Part IV below.
3. Establishing the duration of suffering. This has been calculated from the date of termination and the date of diagnosis of major depressive disorder.

Part II Lost Earnings

For this analysis I am defining the period of lost earnings to be from March 17, 2019, to July 27, 2021. Lost salary, 401k contributions, lost continuing medical education funding, and unawarded academic/administrative days are included in this calculation. Life insurance costs have not been calculated as I understand Dr. Desai is asking Employer to secure an equivalent life insurance policy for Dr. Desai.

Lost Salary

At her the time of her termination, Dr. Desai was earning an annual salary of $340,000.00. Dr. Desai has stated her intention of continuing to work until at least 2029, so future lost earnings are calculated for 10 years. According to the U.S. Bureau of Labor Statistics[1] the inflation rates for March 2019 to February 2020 and March 2020 to July

[1] CPI – for All Urban Consumers, Bureau of Labor Statistics https://data.bls.gov/cgi-bin/surveymost. Updated Jul 2021, accessed Jul 2021

2021 are 1.54% and 5%. The expected annual inflation rate from August 2021 to March 2029 is 1.61%[2]. Additionally, O-Net from the U.S. Department of Labor[3] reports an expected 4% growth in the radiologist profession over the next 10 years. This value is used as a proxy for salary growth from March 2019 until March 2029. Values for lost salary assuming no inflation or salary growth, inflation adjusted, and inflation and salary growth adjusted are reported below.

Lost 401k Contributions

In addition to her salary, earnings also include the value of 401k contributions Dr. Desai received. Dr. Desai reports that UMass Hospital contributed 8% of her salary to her 401k. Without knowing how Dr. Desai's 401k is invested, the lost 401k contributions are calculated using known growth in the S&P 500 from March 2019 to July 2021, and the expected growth rate of the S&P 500 as reported by S&P 500 Global Market Intelligence[4] for the next 10 years. As with the lost salary calculations, the lost 401k contributions are calculated assuming no salary growth, inflation adjusted, and inflation and salary growth adjusted salaries are used for the 401k contributions. The values are reported below.

Lost Academic/administrative days

The value of lost academic/administrative days are calculated with no salary growth, inflation adjusted and inflation, and salary growth adjusted annual salaries. The value of lost academic/administrative days are calculated based on the following equation

$$Value\ of\ Academic\ days = 1.5 * \frac{Salary}{52\ weeks * 5\ days}$$

Values are calculated for 10 years using no salary growth, inflation adjusted, and inflation and salary growth adjusted salaries. The values are reported below.

Lost Continuing Medical Education

The value of lost Continuing Medical Education is calculated assuming an annual value of $4,000.00 per year as reported by Dr. Desai. The values are reported below.

[2] Inflation Expectations, Federal Reserve Bank of Cleveland https://www.clevelandfed.org/our-research/indicators-and-data/inflation-expectations.aspx. Updated Jul 2021, accessed Jul 2021.
[3] O-Net Online 29-1224.0 Radiologist, U.S. Department of Labor https://www.onetonline.org/link/summary/29-1224.00. Updated 2020, accessed Jul 2021
[4] Scheid, Brian, "S&P 500 returns to halve in coming decade – Goldman Sachs", Jul 15 2020, https://www.spglobal.com/marketintelligence/en/news-insights/latest-news-headlines/s-p-500-returns-to-halve-in-coming-decade-8211-goldman-sachs-59439981.

Part III Value of Reduced Quality of Life

Establishing Value of Time

Dr. Desai's value of time is estimated using her salary at the time of termination, as the last mutually agreed upon value of Dr. Desai's time. The value of a day of Dr. Desai's time is calculated using the following equation.

$$value\ of\ a\ day = 24\frac{hours}{day} * (\frac{Salary}{52\frac{weeks}{year} * 40\frac{hours}{week}})$$

Using the equation above, one day of Dr. Desai's time is valued at $3,924.08

Establishing Reduction in Quality of Life

The reduction in quality of life was determined by a close examination of the extant literature on the effects of depression on quality of life. Jia, et al in 2015[5] determined depressive symptoms and quality of life scores for 276,442 individuals. It was determined that the quality of life for all participants was reduced by 33.92%, and 60.74% for the over 65 group.

Steensma et al in 2016[6] used the Canadian Community Health Survey as well as the Health Utilities Index to calculate health related quality of life measures. The authors found that quality of life was reduced by 32.18% for those with depression.

IsHak et al 2015[7] calculate the improvement in quality of life for 2,280 adults following several different interventions. As part of their work the authors calculated that major depressive disorder reduced quality of life by an average of 49.1%

Values of suffering were calculated for each of the reduction in quality-of-life values listed above and are reported below.

Establishing Duration of Suffering

Values of suffering were calculated since the date of diagnosis (5/15/2020) as well as the date of termination (3/17/2019) and are reported below.

[5]Jia, Haomiao, Matthew M. Zack, William W. Thompson, Alex E. Crosby, and Irving I. Gottesman. "Impact of depression on quality-adjusted life expectancy (QALE) directly as well as indirectly through suicide." Social psychiatry and psychiatric epidemiology 50, no. 6 (2015): 939-949.

[6]Steensma, C., L. Loukine, H. Orpana, L. McRae, J. Vachon, F. Mo, M. Boileau-Falardeau, C. Reid, and B. C. Choi. "Describing the population health burden of depression: health-adjusted life expectancy by depression status in Canada." Health promotion and chronic disease prevention in Canada: research, policy and practice 36, no. 10 (2016): 205.

[7]IsHak, Waguih William, James Mirocha, David James, Gabriel Tobia, Jennice Vilhauer, Hala Fakhry, Sarah Pi et al. "Quality of life in major depressive disorder before/after multiple steps of treatment and one-year follow-up." Acta Psychiatrica Scandinavica 131, no. 1 (2015): 51-60.

Part IV Value of Reduced Quality of Life and Lost Earnings

The values reported in this section are raw values and not present value adjusted. Present-value adjusted values are reported in the following section.

Value of Lost Wages

The calculated values for lost earnings are reported below:

No Inflation:	$3,400,000.00
Inflation:	$3,645,456.84
Inflation and Salary Growth:	$3,912,436.69

Value of Lost 401k Contributions

The calculated values for lost 401k contributions is reported below.

No Inflation adjustment in salary:	$3,723,757.00
Inflation adjustment in salary:	$4,253,600.71
Inflation and Salary Growth	$4,820,015.51

Value of Lost Academic/Administrative Days

Total Loss to date:	$239,307.69
Expected Loss:	$778,730.77

Value of Lost Continuing Medical Education

Total loss (to date and expected):	$40,000.00

Value of Reduced Quality of Life

Values are reported assuming Dr. Desai was suffering from major depressive disorder from the moment of her termination, and since the date of the official major depressive disorder diagnosis. As well as, using the reduced quality of life values calculated by Jia, et al (2015) (both total and 65+), Steensma, et al (2016), and IsHak, et al (2015).

Duration	Jia, et al 2015		Steensma, et al 2016	IsHak, et al 2015
	65+	All		
Since 3/17/2019	$10,741,983.84	$5,999,299.28	$5,691,798.41	$6,261,194.06
Since 5/25/2020	$9,705,434.83	$5,420,396.18	$5,142,567.64	$5,423,283.68

Present Value

Once the value of lost future earnings has been established, it must be reduced to present value. That is, one must determine how much money would have to be set aside and invested today to provide that future loss in earnings. The only element that is uncertain in calculating the present value is the net rate of return that will be earned on the funds that are invested for future use. Because the loss of future earnings are estimated using the

current value of the dollar (net of inflation), they are discounted using an expected rate of return that is also real (net of inflation).

The discount rate used here to determine the present value of future lost earnings is calculated using the 10-year treasury rate.[8]

Present Value of Lost Earnings

The calculated values for lost earnings are reported below:

No Inflation:	$3,217,197.29
Inflation:	$3,461,050.14
Inflation and Salary Growth:	$3,708,661.02

Present Value of Lost 401k Contributions

The calculated values for lost 401k contributions are reported below.

No Inflation adjustment in salary:	$3,288,751.16
Inflation adjustment in salary:	$3,756,699.01
Inflation and Salary Growth	$4,256,945.76

Present Value of Lost Academic/Administrative Days

Total Loss	$927,067.85

Present Value of Lost Continuing Medical Education

Total loss (to date and expected):	$35,327.24

Present Value of Reduced Quality of Life

Values are reported assuming Dr. Desai was suffering from major depressive disorder from the moment of her termination, and since the date of the official major depressive disorder diagnosis. As well as, using the reduced quality of life values calculated by Jia, et al (2015) (both total and 65+), Steensma, et al (2016), and IsHak, et al (2015).

Duration	Jia, et al 2015		Steensma, et al 2016	IsHak, et al 2015
	65+	All		
Since 3/17/2019	$9,725,952.26	$5,431,854.97	$5,153,439.10	$7,862,123.50
Since 5/25/2020	$8,689,403.24	$4,852,951.87	$4,604,208.33	$7,024,213.12

Summary of Findings

Based on the information I have available at the present time; I have formed an opinion to a reasonable degree of economic certainty that Dr. Desai's present value losses to date range from $1,535,807.33 to $6,081,293.11. Her present value future losses range from $10,536,744.55 to $12,572,661.02. Dr. Desai's present value present and future losses because of her termination and the resulting major depressive disorder diagnosis range

[8] Treasury yields

from $12,072,551.88 to $18,653,954.13. These values are calculated based on lost earnings, 401k contributions, academic/administrative days, continuing medical education fund and reduced quality of life associated with a diagnosis of major depressive disorder. These values are calculated assuming Dr. Desai would have worked an additional 10 years beyond her date of termination.

This opinion is based on the information I have at this time. I reserve my right to supplement this opinion as any new information becomes available that would materially change the damages in the case such as changes in interest rates, a change in Dr. Desai's current or additional diagnoses, or a change in actual or expected inflation rates.

As required by Federal Rule 26(b) regarding the opinions of expert witnesses I state the following:

In forming my opinion in this matter I have relied upon the following information:

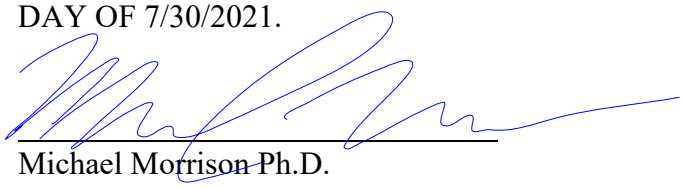
1. Information provided by Patricia A. Washienko, Esq., set out in Appendix A.
2. Information from public published sources as footnoted in my report.

Attached is a copy of my current curriculum vita, which includes a list of all my publications in the last 10 years.

I hereby state that I am being compensated as an expert in this case at the rate of $1,750 for this report and $350 per hour for any additional work. I have spent approximately 6 hours up to this point on this case.

Attached is a copy of cases that I have testified in over the past 4 years and it is current as of this date.

SIGNED UNDER THE PAINS AND PENALTIES OF PERJURY ON THIS DAY OF 7/30/2021.



Michael Morrison Ph.D.

Michael Morrison Ph.D.
Economic consulting

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Tel: 505-231-0041
Mtmichael@gmail.com

Economic Report - Addendum

To: Patricia A. Washienko, Esq.

From: Michael Morrison Ph.D.

Date: 07/27/2021

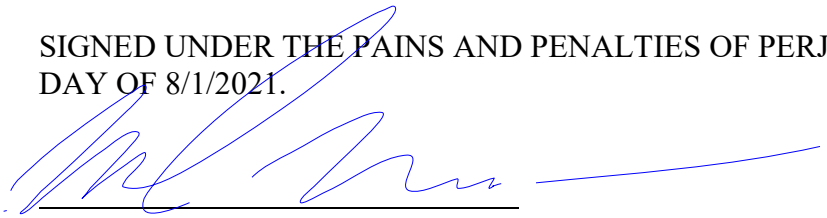
Re: *Dr. Desai v. UMass Memorial Health, et al.*

Addendum

Dr. Desai's termination and major depressive disorder diagnosis forced Dr. Desai's husband, Shirish Desai, to prematurely retire as well. Mr. Desai had also planned to work for an additional 10 years. At his current salary of $150,000 per year. The present value of total lost salary is between $1,419,351.75 and $1,570,077.18. Lost salary values are calculated based on the assumption of no salary growth and inflation adjusted annual salary. Values for actual and expected inflation are the same as in the main report.

I hereby state that I am being compensated as an expert in this case at the rate of $1,750 for the main report and $350 per hour or the addendum and any additional work. I have spent approximately 1 hour on this addendum and 7 hours total on this case.

SIGNED UNDER THE PAINS AND PENALTIES OF PERJURY ON THIS DAY OF 8/1/2021.



Michael Morrison Ph.D.

Previous Cases:

I have not testified in any cases as of July 28, 2021

I have provided an Economic Impact Report for Tim Kolman, Esq. for an EEOC complaint.

Appendix A

Charu Desai was born on July 6, 1950. She resides in Worcester, Massachusetts.

Dr. Desai is a radiologist. She began working at UMass in the Department of Radiology in 1992. Dr. Desai was informed of her termination on March 17, 2018. Her termination became effective March 17, 2019.

As of the effective date of Dr. Desai's termination, she had worked at the UMass entities for 27 years. She planned to finish out her career there. She had no immediate plans to retire; rather, she expected to work at least ten (10) more years (i.e., until March 2029, when she would be 78 years of age).

At the time of her termination, Dr. Desai was paid an annual salary of $340,000. Dr. Desai believes that her employer matched her 401(k) contribution at 8%.

Throughout her employment, Dr. Desai also received life insurance coverage. Due to her age and health condition, it is cost prohibitive for her to purchase comparable life insurance (a $50k death benefit) on the open market. (As part of her damages / part of the resolution of this matter, Dr. Desai seeks to secure a life insurance policy in the amount of $50,000 from Defendants, or, alternatively, that Defendants provide her with payment in that amount.)

Dr. Desai has incurred losses in the amount of approximately $9,000 in lost Continuing Medical Education Fund benefits ($4,000 annually).

Dr. Desai was not awarded "academic days" on which days she would not have been required to perform clinical duties. Younger doctors were granted academic days. A younger radiologist, who was hired three years before Dr. Desai's termination, was given one and one-half academic and/or administrative days per week (i.e., 78 per year).

Dr. Desai also is aware that another younger co-worker was paid $10,000 per year more than her since 2016.

Since her termination, Dr. Desai has diligently searched for another radiology position but has not secured or even been offered one.

In March 2019, Dr. Desai's husband, also a medical doctor, stopped doing locum tenens work, for which work he earned approximately $150k annually, to care for her, as she was so distressed by her termination it impacted her day-to-day functioning. He has not performed any locum tenens work since then.

Dr. Desai was diagnosed on 5/25/2020 with major depressive disorder and has been in the care of a psychiatrist (and on medication) since that time.

Michael Morrison
Assistant Professor
5205 Caprock Dr.
Rio Rancho, NM 87144
Home: (505)231-0041, Office: (814)731-1657
Email: mmorrison@edinboro.edu

EMPLOYMENT HISTORY

Assistant Professor (tenured) at Edinboro University of Pennsylvania (August 2013-Present)

EDUCATION

Ph.D. Economics, University of New Mexico, Albuquerque, NM August 2013
M.A. Economics, University of New Mexico, Albuquerque, NM August 2012
B.S. Economics, Montana State University, Bozeman, MT 2004

DISSERTATION **The Law of One Price and Virtual Worlds**

Part I. "Virtual World Research in the Social Sciences"
Part II. "Price Convergence after Cataclysm"
Part III "STAR modeling of Band of Inaction Variations"
Committee: Prof. Matías Fontenla (Co-Chair), Prof. Christine Sauer (Co-Chair), Prof. Alok Bohara, Prof. Christopher Butler

FIELDS OF SPECIALIZATION

Primary: International Economics
Secondary: Development Economics and Environmental Economics

PUBLICATIONS AND PAPERS

Publications

Morrison, Michael, and Matías Fontenla. "Price Convergence in an Online Virtual World." Empirical Economics (2013): 1-12.
Morrison, Michael and Matías Fontenla. "Purchasing Power Parity across Eight Worlds," Economics Letters 158 (2017): 62-68.

Works in Progress

Morrison, Michael and Christine Sauer. "Band of Inaction Variations in Response to Changes in Transaction Costs," Working Paper
Morrison, Michael and Scott Duda. "The Balance of Payments and the Band of Inaction," Working Paper
Morrison, Michael. "The Harrod-Balassa-Samuelson Effect and the Band of Inaction," Working Paper.
Morrison, Michael and Kyle Hurysz. "Impact of BP Oil Spill on Aggregate Transportation Costs," Working Paper.
Dexter, John, Michael Morrison, Da Ler, and Tara Lambert. "Increasing the Likelihood of Sitting for the CPA Examination: Effects of Incorporating CPA Review Course Materials in Intermediate Accounting Classes," Working Paper

Conference Presentations

Morrison, Michael and Christine Sauer, "The Variable Band of Inaction: Transaction Costs and the Size of the Band of Inaction," Southwestern Social Science Association 2018 Annual Meeting, Orlando, FL 2018
Morrison, Michael and Dennis Barber III, "What can Virtual Behavior offer to Entrepreneurship Education," Southeast Decision Science Institute, Savannah, GA 2015
Morrison, Michael and Dennis Barber III, "Does the EAO Remain Valid in the Virtual World," Pennsylvania Economic Association Conference, Edinboro, PA 2014
Morrison, Michael and Matías Fontenla "Price Convergence After Cataclysm," 56th annual Western Social Science Association Conference, Albuquerque, NM 2014

Morrison, Michael and Christine Sauer, "Variable Band of Inaction: Transaction Costs and the Size of the Band of Inaction," 56th annual Western Social Science Association Conference, Albuquerque, NM 2014

Morrison, Michael and Matías Fontenla, "Price Convergence in an Online Virtual World," 91st annual Southwestern Social Science Association Meeting, Las Vegas, NV. 2011

Morrison, Michael "Estimating and International Property Rights Value for Haiti," 51st annual Western Social Science Association Conference, Albuquerque, NM. 2009

Morrison, Michael "Testing the Purchasing Power Parity Hypothesis within an Online Virtual Economy," 89th annual Southwestern Social Science Association Meeting, Denver, CO. 2009

Other Presentations

Morrison, Michael and Matias Fontenla. "Purchasing Power Parity across Eight Worlds," Edinboro University Academic Festival, Edinboro, PA 2017

Morrison, Michael "Price Convergence after Cataclysm" Faculty Research Presentation at Porreco, Erie, PA 2016

Morrison, Michael "Unemployment in the U.S. Structural or Cyclical?" Al Stone Lecture Series, Edinboro, PA 2014

Morrison, Michael and Matías Fontenla, "Price Convergence after Cataclysm," Department of Business and Economics Research Symposium Series, Edinboro, PA. 2013

TEACHING EXPERIENCE

International Finance, Edinboro University of Pennsylvania, fall 2018-present
Econometrics, Edinboro University of Pennsylvania, spring 2015-present
International Economics, Edinboro University of Pennsylvania, spring 2014-present
Economic Development, Edinboro University of Pennsylvania, fall 2013-present
Principles of Macroeconomics, Edinboro University of Pennsylvania, 2014- present
Principles of Microeconomics, Edinboro University of Pennsylvania, fall 2013-spring 2018
Career Preparation Seminar, fall 2015-spring 2016
Business Primer, Edinboro University of Pennsylvania, fall 2014, fall 2016
Intermediate Macroeconomics, University of New Mexico, summer 2011–fall 2012
Introductory Macroeconomics, University of New Mexico, spring 2010–winter 2012.

RESEARCH/WORK EXPERIENCE

Research Assistant, David Brookshire, Albuquerque, NM, summer 2008-fall 2009
Responsibilities included assisting, in implementation of economic experiments, designing, printing and distributing an online and mail contingent valuation method (CVM) and choice experiment (CE) survey.

PROFFESIONAL HONORS

Nominated for Faculty Member of the Year at Edinboro University of Pennsylvania, 2016-2017 academic year.
Southern Economic Association sponsored graduate student presentation, $155, November 2012

RESEARCH FUNDING

Research Travel Projects Grant, Office of Graduate Studies University of New Mexico, "Price Convergence in a Virtual World, March 2011, $700

SERVICE

Expert Witness for Kolman Law P.C. Summer 2021
Project Lead/Primary Contributor ACBSP decennial re-accreditation report Fall 2020
Assistant Department Chair, Department of Business and Economics, summer 2017-present
Chair, Elections and Nominations Committee, APSCUF (faculty union) spring 2019-

present
Member, Board of Directors, Erie Humane Society (formerly Humane Society of Northwest Pennsylvania), spring 2019 - present
Faculty Member, Presidential Working Group #2, spring 2017
Co-Adviser, Business and Economics Club, spring 2016 - present
Adviser, Alpha Kappa Psi – Business Fraternity, spring 2016- present
Co-Adviser, Delta Mu Delta – Business Honor Society, spring 2016 - presents
Founding member, Humanity and Sustainability Institute, fall 2015-present.
Co-Chair, General Education Redesign Task Force, Edinboro University of Pennsylvania, fall 2013-summer 2016.
Referee, Energy Economics 2014
Student Recognition Committee, Department of Business and Economics, Edinboro University of Pennsylvania, fall 2013-Present.
Economics Comprehensive Exam Committee, Department of Business and Economics, Edinboro University of Pennsylvania, fall 2013-Present.
Sabbatical Leave Committee, Department of Business and Economics, Edinboro University of Pennsylvania, fall 2013-Present.
Department Secretary, Department of Business and Economics, Edinboro University of Pennsylvania, fall 2013-spring 2014.
Referee, Applied Economics – 2011, 2019

CURRICULUM DEVELOPMENT

Co-Presenter, Center for Faculty Excellence, "Teaching Critical Thinking Effectively," Edinboro University of Pennsylvania, September 2018 and February 2019.
Participant, OSET Workshop, "Designing Courses for Effective Student Learning," UNM, May 2010 and August 2011.

TECHNICAL SKILLS

STATA, RATS, MS OFFICE GNUPLOT, SPSS, SQL

MEDIA APPEARANCES

Wired Magazine, "Bot Mafias Have Wreaked Havoc in *World of Warcraft Classic*," June 17, 2020. https://www.wired.com/story/world-of-warcraft-classic-russian-bots/

Published in final edited form as:
Acta Psychiatr Scand. 2015 January ; 131(1): 51–60. doi:10.1111/acps.12301.

Quality of Life in Major Depressive Disorder Before/After Multiple Steps of Treatment and One-year Follow-up

Waguih William IsHak, MD, FAPA,
Department of Psychiatry and Behavioral Neurosciences, Cedars-Sinai Medical Center, and Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine at University of California Los Angeles (UCLA), Los Angeles, California, United States.

James Mirocha, M.S.,
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Abstract

Objective—This study examines the impact of Major Depressive Disorder (MDD) and its treatment on Quality of Life (QOL).

Method—From the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial, we analyzed complete data of 2,280 adult MDD outpatients at entry/exit of each level of antidepressant treatments and after 12-months of entry to follow-up. QOL was measured using the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). The proportions of patients scoring 'within-normal' QOL (within 10% of Q-LES-Q community-norms) and those with 'severely-impaired' QOL (>2SD below Q-LES-Q community-norms) were analyzed.

Results—Before treatment, no more than 3% of MDD patients experienced 'within-normal' QOL. Following treatment, statistically significant improvements were detected, however the proportion of patients achieving 'within-normal' QOL did not exceed 30%, with>50% of patients experiencing 'severely-impaired' QOL. Although remitted-patients had greater improvements compared to non-remitters, 32%-60% continued to experience reduced QOL. 12-month follow-up data revealed that the proportion of patients experiencing 'within-normal' QOL show a statistically significant decrease in non-remitters.

Conclusion—Symptom-focused treatments of MDD may leave a misleading impression that patients have recovered when, in fact, they may be experiencing ongoing QOL deficits. These findings point to the need for investigating specific interventions to ameliorate QOL in MDD.

Keywords

Quality of Life; Major Depression; Antidepressants; Functional Outcomes; Patient-reported outcomes

INTRODUCTION

According to the World Health Organization (WHO), quality of life (QOL) represents the individual's subjective evaluation of physical, mental, and social domains (1). Major depressive disorder (MDD), which is the leading cause of disability globally affecting nearly 350 million people worldwide (2), is associated with substantial deficits in QOL (3,4). Importantly, QOL deficits have been shown to persist beyond the clinical resolution of symptoms (5), placing patients at an increased risk for relapse and rising direct and indirect costs (6). A poor QOL often overlaps with depressive symptom severity (7). However, a number of studies have shown that the severity of depressive symptoms explained only a small proportion of the variance in QOL (3, 4, 8). These findings suggest that assessing symptom reduction alone may not be the best way to gauge the success of MDD interventions. Despite being increasingly recognized as an important measure of health in

medical and psychiatric patients (9, 10), QOL needs to be given more attention in clinical and research efforts in MDD.

To fully assess the impact of MDD and its treatment on QOL, we analyzed QOL data from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial (11, 12), the largest prospective randomized study of treatment effectiveness for outpatients with MDD. Previous STAR*D reports have already shed some light on QOL in MDD (13, 14). Trivedi and colleagues found that greater MDD symptom severity was statistically significantly associated with reduced QOL, and that socio-demographic factors such as race, education, employment, and medical insurance status, as well as general medical and depressive illness were independently associated with poorer QOL (13). Daly and colleagues further examined QOL across psychological, physical, and social domains, showing low correlations between these three domain measures, suggesting that they evaluate different and non-overlapping aspects of function (14). However, the full details of the pre-treatment QOL, the immediate and long-term impact of treatment on QOL, and the clinical significance of the aforementioned themes remain to be investigated. Moreover, studies examining what depressed patients ranked as important goals for treatment revealed that patients hope to return to ‘normal’ levels of functioning and QOL (15). Research seems to point to the notion that patients and clinicians seem to expect this normalization after achieving remission (15), an idea that has yet to be examined. We know very little about the proportions of patients with ‘normal’, i.e., close to community norm QOL scores, before and after treatment. This present analysis examines QOL at entry and exit of each of the four levels of the acute treatment phase as well as the 12-months follow-up phase of the STAR*D study. We hypothesized that:

1. Prior to treatment, MDD patients will report statistically significant QOL deficits, defined as the minority of patients reporting ‘within-normal’ QOL and the majority reporting ‘severely-impaired’ QOL.
2. QOL will show statistically significant improvement with each treatment level, however a proportion of patients will continue to experience the aforementioned QOL deficits immediately after acute treatment.
3. After 12 months, patients who achieved MDD remission will experience higher QOL scores, perhaps close to those seen in community norms.

Aims of the study

The aim of the study is to examine Quality of Life at the entry and exit of each of the four levels of the acute treatment phase as well as the 12-months follow-up phase of the STAR*D study.

Material and methods

Study Population

Funded by the National Institute of Mental health (NIMH), the STAR*D study was conducted at 18 primary care and 23 psychiatric care centers in the United States. STAR*D enrolled 4,041 treatment-seeking outpatients aged 18–75 between 2001 and 2007, all

carrying a primary diagnosis of MDD. Full details of the study's methodology are described elsewhere (11, 12). The authors of the present study obtained an NIMH Data Use Certificate to utilize the STAR*D Public Ver3 dataset. To be eligible for the present analysis, participants needed to have complete data for each of the outcome measures detailed below, at both entry and exit for each level of the study. Patients who were in remission at the beginning of each level were excluded. The analyzed dataset of this study contained 2,280 Level1-participants, 749 Level2-participants, 190 Level3-participants, 56 Level4-participants, and 414 participants from all levels at 12-months follow-up.

Treatments Administered

The treatment interventions are detailed elsewhere (11, 12). Briefly, treatments were administered according to a fixed-flexible dosing schedule and modified based on each participant's response. Patients were moved to the next level if they did not achieve remission. Participants were enrolled into the following STAR*D levels:

Level 1: Citalopram monotherapy.

Level 2: Switching to sertraline, sustained-release (SR) bupropion, extended-release (XR) venlafaxine, or Cognitive Behavioral Therapy (CBT) OR Augmenting with bupropion SR, buspirone, or CBT.

Level 3: Switching to nortriptyline or mirtazapine OR Augmenting with lithium or Triiodothyronine (T3).

Level 4: Switching to tranylcypromine OR Switching to venlafaxine XR + mirtazapine.

The study used an equipoise stratified randomized design which allowed patients a choice between several switch or augmentation strategies, within the permissible limits of the study design. This approach was adopted in lieu of complete randomization in order to mimic clinical practice (16). During the follow-up phase, patients were strongly advised to continue taking the previously effective drug(s) (17).

Outcome Measures

QOL was assessed using the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) (18). The Q-LES-Q is a self-report instrument that measures satisfaction and enjoyment in a series of discrete domains of functioning such as mood, social relationships, living or housing situation, and physical health. This study uses the short version, which has 16 items, each scored on a 5-point Likert scale. Summing up the results of the 14 first items, then dividing by the maximum possible score and multiplying the figure by 100 gives a total score ranging from 0 to 100, with 0 being lowest QOL score and 100 the highest. Community norm samples have a mean Q-LES-Q score of 78.3 (SD=11.3) and scores within 10% of this value, i.e., Q-LES-Q≥70.47, are considered 'within-normal' QOL (1), which corresponds with the 75th percentile. Q-LES-Q scores greater than 2 SD below the community norm scores, i.e., Q-LES-Q scores≤55.7, are considered 'severely-impaired' QOL (19), which corresponds with 95th percentile. The Q-LES-Q has shown moderately negative correlations with the Clinical Global Impressions–Severity of Illness scale (CGI-S) ($r = -0.62$ for the summary scale) and the 17-item Hamilton Rating Scale for Depression ($HRSD_{17}$) ($r = -0.61$ for the summary scale). The Q-LES-Q also has strong psychometric

properties (Cronbach's α=0.90, test-retest reliability r=0.74) (18). Although STAR*D did include the SF-12 as another QOL/Functioning instrument, a number of limitations (with the SF-36 and its abbreviated version, SF-12) precluded its use for our purpose in studying QOL, the most important of which are: the confusion/mix-up in asking patients to self report functioning level in lieu of QOL, and the equal emphasis on physical and mental components of health status (4). Therefore, we limited the analysis to using the Q-LES-Q.

MDD symptom severity was measured using the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR) (0 =not depressed to 27=most depressed) with remission is defined as a score≤5 (20). The QIDS-SR is highly correlated with all three versions of the widely utilized clinician-rated Hamilton Rating Scale for Depression, the Montgomery Åsberg Depression Rating Scale, and the Beck Depression Inventory, with a high internal consistency; Cronbach's alpha =0.86 (20).

Statistical Methods

The variables were assessed and confirmed to have normal distribution. Summary values are expressed as means and standard deviations (SD) for continuous variables, and frequencies (%) for categorical variables. The paired t-test was used for comparisons between entry and exit numerical outcomes, within each level. Effect sizes were calculated for the outcomes (21), in which Cohen's d values of 0.2, 0.5, and 0.8 describe small, medium, and large effects, respectively (22). Since we calculated Cohen's d values in paired samples pre and post treatment, effect sizes were corrected for correlated designs as detailed by Dunlap et al. in 1996 using Equation 3 (23). Entry to exit comparisons of binary variables within each level and follow-up, were assessed using the exact version of the McNemar test for related proportions. The proportions of patients that scored 'within-normal' on the relevant measures were compared between remitters and non-remitters at exit, using the Chi-square test (or Fisher exact test for small sample sizes). Given the number of performed tests, we used a Bonferroni-adjusted 0.01 significance level for each test. Analyses were performed using SAS software, version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

Study Population Demographics

The demographic characteristics of the analyzed patient sample (n=2,280) are shown in Table 1. At baseline, women constituted nearly two thirds of the study population, the majority of patients were Caucasian, more than one half were employed, and about one third were college graduates. The demographic characteristics of the analyzed sample were comparable to those of the whole STAR*D sample.

Mean Scores on Measures of Depressive Symptom Severity, and Quality of Life

STAR*D level-by-level, pre and post-treatment QOL scores (Q-LES-Q), and depressive symptom severity (QIDS-SR), in addition to scores at entry and exit from the 12-months follow-up phase, are displayed in Table 2.

Patients in the acute treatment phase in each level made statistically significant improvements on both measures. Changes in depressive symptom severity (QIDS-SR scores) showed the following effect sizes (Cohen's *d*) at the end of each level of treatment: *d*=1.05 at Level1, *d*=0.65 at Level2, *d*=0.42 at Level3, and *d*=0.71 at Level4 ($p<0.001$ for all). Changes in QOL, as indicated by differences in pre- and post-treatment scores on the Q-LES-Q, had the following effect sizes: Level1 Cohen's *d*=0.78 ($p<0.001$), Level2 *d*=0.52 ($p<0.001$), Level3 *d*=0.20 ($p=0.002$), and Level4 *d*=0.41 ($p=0.001$).

Interestingly, patients at 12-month follow-up showed statistically significant deterioration on both measures with effects sizes of QIDS-SR Cohen's *d*=-0.43 ($p<0.001$), and Q-LES-Q *d*=-0.38 ($p<0.001$).

It is also important to note that at baseline of Level1, the Pearson's correlation coefficient *(r)* between the QIDS-SR and the Q-LES-Q is 0.74.

Proportions of Patients with 'Within-normal' Quality of Life Scores

STAR*D level-by-level and 12-months follow-up, entry and exit proportions of patients exhibiting 'within-normal' QOL (Q-LES-Q≥70.47) are displayed in Table 3.

At entry to any level, no more than 3% of MDD patients experienced 'within-normal' QOL. Although treatment increased the number of patients achieving 'within-normal' QOL scores, the majority of patients (70.9%) scored lower than the 'within-normal' QOL range.

Nearly 46.4% of follow-up patients were in remission after 12 months of completing acute treatment. The proportions of follow-up patients experiencing 'within-normal' scores for QOL at 12 months decreased from the time of acute treatment phase completion: from 46.6% to 31.6% ($p<0.001$).

Proportions of Patients with 'Severely-Impaired' Quality of Life Scores

Level-by-level, pre- and post-treatment in addition to entry and exit follow-up percentages of patients with 'severely-impaired' QOL (two SD below community norms, i.e., Q-LES-Q = <55.7) are displayed in Table 3.

QOL data, at all treatment levels, revealed that the majority (>80%) of MDD patients experienced 'severely-impaired' QOL at entry. The data also shows that treatment statistically significantly decreased the number of patients with 'severely-impaired' QOL at the end of each level. For instance, at the end of Level1, the percentage of patients experiencing 'severely-impaired' QOL decreased from 85.6% to 50.5% ($p<0.001$). However, consistent with the above findings on 'within-normal' scores, sizable proportions of patients were still left with 'severely-impaired' QOL, ranging from 50 to 70%.

The proportions of follow-up patients experiencing 'severely-impaired' QOL showed a statistically significant increase from 28.5% at entry to follow-up, to 42.5% after 12 months ($p<0.001$).

Proportions of Remitters vs. Non-Remitters with 'Within-Normal' Quality of Life Scores

Remission from MDD is defined as experiencing minimal symptoms or none at all, as measured by QIDS-SR score≤5 (20). As detailed in Table 4, remission was associated with a statistically significant increase in the proportion of patients experiencing 'within-normal' QOL (Q-LES-Q scores) after each level of treatment. However, despite meeting remission criteria, 30–60% of patients did not achieve 'within-normal' QOL scores at exit. Similarly, Table 4 shows that the proportion of patients with 'severely-impaired' QOL showed a statistically significant decrease, especially in remitters. Nevertheless, 9–43% of remitters still scored in the 'severely-impaired' QOL range.

The proportion of follow-up patients with 'severely-impaired' QOL or 'within-normal' QOL scores did not statistically significantly change after 12 months in remitted patients. In contrast, non-remitters showed a statistically significant decrease in proportions of individuals with 'within-normal' QOL scores (from 31.8% to 7.7%; $p<0.001$) and increased proportions of patients with 'severely-impaired' QOL (from 41% to 68%; $p<0.001$).

DISCUSSION

The present study has a number of important findings: Firstly, MDD patients reported statistically significant QOL deficits, i.e., both high proportions of 'severely-impaired' QOL (i.e. >2SD below community norms), and low proportions of patients scoring within the community norm of QOL scores at the entry of each STAR*D level. Secondly, treatment was associated with statistically significant improvement in QOL, although the majority of all MDD patients continue to experience lower QOL than the general population, with a low proportion of them scoring 'within-normal' QOL; in addition, at each level, patients who achieved remission showed greater improvements in QOL compared to their non-remitting counterparts, yet a sizable proportion of remitted MDD patients did not achieve 'within-normal' QOL scores. Thirdly, follow-up data show that the mean QOL scores of all patients declined after 12 months, as did the proportion of overall patients experiencing 'within-normal' scores; an effect that was only statistically significant in non-remitters.

With no more than 3% of STAR*D entry patients—at any level—reporting 'within-normal' QOL, treating MDD poses a tremendous challenge, not only in treating depressive symptoms but also in ultimately improving QOL. Previous studies have shown that QOL is impaired in MDD and that depression severity is a major contributor to poor QOL (3, 4). It has been postulated that there is a bidirectional relationship between QOL and MDD where MDD could lead to poor QOL and vice versa, in addition to the possible negative influence of depression influence on self evaluation including rating one's own QOL (24–26). Our study shows a strong correlation between the QIDS-SR and the Q-LES-Q of 0.74. In other analyses that examined baseline QOL in MDD data, although moderate to high correlations between depressive symptom severity and QOL were detected, regression analyses showed that the former (as measured by the QIDS-SR) accounted for only 48% of the variance in QOL (as measured by the Q-LES-Q) (4). Reduced QOL in depressed patients may be associated with problems with financial issues, family or social relationships, living situation, or physical health. Earlier pre-treatment analyses of the STAR*D study revealed

that socio-demographically disadvantaged patients with greater general medical and depressive illness burden were at greatest risk for poor QOL (13, 14).

One of the primary objectives of the present study was to determine the extent to which observed deficits in QOL in MDD patients could be improved by treatment, and whether the progress could be maintained at 12 months. Our findings indicate that QOL shows statistical significant improvements when MDD is treated, especially in symptom severity and QOL, with the largest effect sizes observed after the first treatment trial (Level1). However, fewer than 30% of patients exiting Level1 of treatment – both remitters and non-remitters - achieved ‘within-normal’ QOL scores. Additionally, more than 50% of these same patients had ‘severely-impaired’ QOL. Low overall remission rates (e.g. 35% at Level1) may partially explain why most patients continued to experience QOL deficits following treatment.

Our findings reveal that remitted patients showed a remarkable change in the proportions achieving ‘within-normal’ QOL scores after treatment. Of note, 68% of remitted patients at the end of Level 1 treatment reported 'within normal' QOL; a proportion that is not markedly different from the proportion expected for the healthy population. This finding points out to the positive QOL gains that could be made in the early stages of treatment. More strikingly, after 12 months of follow-up, the proportion of patients experiencing ‘within-normal’ QOL scores decreased in non-remitters, a trend not observed in remitters. These findings, coupled with previous studies which had reported that patients who failed to achieve complete symptomatic remission often continued to have psychosocial impairment and were more likely to relapse into full depression (27), reinforce the notion that remission (minimal or no symptoms), as opposed to response (typically 50% reduction in severity), should be one of the primary goals of MDD treatment.

Furthermore, our results suggest that treatment should strive to achieve more than mere symptom resolution or remission. A good proportion of remitted patients still had QOL deficits after treatment. Similar deficits in remitted patients have been reported by Angermeyer and colleagues (5), who stated that remitted patients’ QOL scores remained lower than those observed in non-depressed controls, after seven months following discharge for a depressive episode hospital admission. As some remitted patients may return to a perfectly normal social life, others may experience trouble readjusting to their occupational responsibilities in the wake of their depression. These ongoing deficits imply that remitted patients could remain dissatisfied and feel incapacitated across multiple life domains—even after an otherwise clinically successful treatment regimen.

The expectation that QOL could improve spontaneously after symptom remission was not fully supported by the 12-month follow-up data analysis in this study. On the contrary, QOL suffered from statistically significant deterioration specifically in non-remitters, whereas it did not change from entry to follow-up in patients who maintained remission. The above findings are consistent with the literature on long-term follow-up of QOL in MDD (5, 6).

Evidence suggests that improving QOL is an important treatment target for patients with MDD (25). Zimmerman and colleagues examined the outcomes that patients think are

important when treating their MDD (15). Three factors were found to be better indicators of remission than the mere absence of depressive symptoms: the presence of positive mental health, such as optimism and self-confidence, a return to one's usual, normal self, and a return to normal levels of functioning at home, work, or school (15).

Taken together, the findings suggest that while clinicians should target remission as an initial goal of treatment, they need to subsequently extend their interventions to focus on the specific issues where patients continue to experience difficulty, such as QOL and its domains, notwithstanding the contributing factors highlighted above. Interventions that appear in published original research and/or literature reviews, and are postulated to improve QOL include: cognitive behavioral therapy (28), future-directed therapy (29), combined psychotherapy and pharmacotherapy (30), occupational/vocational therapy (31), dopaminergic agents (32), nutrition and nutritional supplements (33), augmentation with omega-3 (34), exercise (35), meditation and yoga (36), humor (37), massage (38), and music (39). QOL interventions could also include the treatment of possible comorbid medical and psychiatric conditions (40, 41), and treatment of sexual dysfunction (42, 43). However, randomized, controlled, large sample studies need to be conducted to confirm the above interventions' usefulness in MDD. An additional approach to improving QOL consists of identifying and compiling the items poorly rated by patients on baseline QOL measures and utilizing them to guide the creation and implementation of a personalized treatment plan containing interventions to address each impaired domain. A wraparound approach to MDD care, combining the efforts of primary care physicians, specialists, nursing staff, social workers and therapists is an option that could be considered (44). Incorporating QOL measurement and monitoring into clinical practice is becoming a vital component to personalize treatment as detailed above. Newly introduced burden of illness measures incorporating symptom severity, functioning, and QOL, such as the Individual Burden of Illness Index for Depression (IBI-D) (45), represent measurement methodologies that may provide more clinically relevant information.

In summary, increased emphasis should be placed on functional outcomes such as QOL, as important, and perhaps the ultimate, indicators of successful treatment (24–27).

Limitations and Strengths

Our study has a number of limitations, some are related to the STAR*D study and some are related to our own analysis. The lack of data on patients who dropped out could have potentially provided useful information about their QOL. Younger patients, African-Americans, those with lower education, and individuals with lower income were shown to be more likely to drop out of the STAR*D study (46,47). Medical predictors of attrition included higher side effects and a higher number of Axis I comorbidities. Previous analyses showed that attrition in the first two steps of the STAR*D study was in the vast majority of cases motivated by non-medical reasons; 92% and 90% respectively (47, 48). Attrition makes it difficult to generalize the conclusions from the sample studied. In the future, it would be important to analyze dropout data in order help us better understand the nature of these patients' struggles. The lack of a control group in the STAR*D study, deprived us from useful comparative data. Another limitation involves the challenge of translating the

above research findings into clinical practice. Administering QOL measures, and acting on their findings, must be balanced against the time-constraining realities of modern practice, however QOL improvement is becoming an established treatment goal in many areas of medicine such as ophthalmology (49) and cardiology (50).

The reliance on self-report raises questions about magnification or minimization of ratings, however patient reported outcomes (PRO) using valid and reliable instruments, such as the ones used in STAR*D, is a growing movement in healthcare and is widely supported by NIH PROMIS, WHO, and the FDA PRO initiatives, as well as clinicians and researchers alike. In this analysis we described QOL using both continuous and categorical approaches. A number of authors had criticized categorizing continuous variables (51, 52). We first examined continuous data to detect changes in depressive symptom severity and QOL using statistical significance parameters with effect sizes, and then we examined two categorical variables derived from QOL scores. Although one could never ascertain pre-morbid QOL, we acted on feedback from patients concerning their need for “normalization” of functional outcomes (15). Therefore, we categorized both variables ‘within-normal QOL’ and ‘severely-impaired’ QOL based on parameters identified in previously published research work (3, 19), similar to when depressive symptoms are categorized as “remission” or “response” according to a cutoff score. Another limitation concerns the fact that our study is a post hoc analysis; therefore the study findings should be considered hypothesis-generating and would need to be replicated in prospective randomized placebo-controlled clinical trials. A possible additional limitation of the study concerns the possible paradoxical impact of pharmacological interventions on QOL. Although antidepressants and other drugs are generally safe and well tolerated, the adverse effects associated with medications could negatively impact QOL and thus mitigate their otherwise positive overall effect (53). Additionally, although follow-up patients were strongly encouraged to continue their effective medications, one could not be absolutely sure that the patients completely followed this directive, especially in the absence of medication-level monitoring in this study.

Ethical considerations of clinicians making judgments about patients’ QOL to guide provision of services have long been debated in medicine (54). Moreover, administering questionnaires that might add to the emotional burden of depressed patients recognizing the magnitude of their QOL deficits, have also been debated from an ethical perspective (55).

One of the strengths of the present study is that it distinctly details pre and post-treatment and 12-months follow-up QOL data from a large population of treatment-seeking MDD patients. “Statistically significant" findings, often reported in the literature as indicated by *p* values, which do not adequately inform the reader about the relevance to the findings observed in daily practice or research settings (56), therefore we included the calculation of effect sizes as indicated by Cohen’s *d* (57). An additional strength is the fact that this population of treatment-seeking MDD patients, recruited from primary care and psychiatry specialty clinics, is representative of what clinicians see in outpatient settings. The findings can be extrapolated to everyday practice, with the one caveat that the majority of patients are Caucasians, which limits the applicability of this analysis to ethnic groups such as African-American, Hispanic, Asian, or Native-American patients. Future research effort to study QOL in minority groups is critically needed.

CONCLUSION

The present analysis highlights the major pitfalls associated with MDD treatments that are purely symptom-focused. Such treatments can give the misleading impression that a patient has recovered, when in fact the patient continues to experience ongoing deficits in QOL. QOL did not improve further after the acute treatment phase even in remitters, and non-remitters showed a statistically significant decline at follow-up after one year. Consequently, clinicians and researchers need to move beyond the mere assessment of symptoms when treating and/or researching MDD, by incorporating QOL measurement, and by investigating specific and personalized interventions to ameliorate QOL.

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Significant Outcomes

- An analysis of 2,280 adult Major depressive disorder patients showed extensive and statistically significant decreased quality of life prior to treatment.
- Treatment had a statistically significant positive impact on quality of life. Nevertheless a majority of patients continue to experience quality of life deficits
- Quality of life scores declined after 12 months, as did the proportion of overall patients experiencing ‘within-normal’ scores.

Limitations

- The study lacked a placebo arm, and this post hoc analysis relied on self-reported outcomes.
- Possible paradoxical impact of pharmacological interventions on quality of life cannot be excluded.

Table 1

Demographic and Baseline Characteristics of the STAR*D Analyzed Sample with Major Depressive Disorder (MDD)

STAR*D Subjects with Complete QOL and Symptom Severity Data Number of Subjects=2,280	
Age range	18.1 – 75.6
Demographics: n (%)	
	2,280 (100%)
Mean Age (SD)	42.6 (13.0)
Female	1,432 (62.8%)
Caucasian	1,846 (80.9%)
Hispanic	239 (10.5%)
College Graduate	686 (30.1%)
Employed	1301 (57.1%)
Living with Spouse/Partner	1046 (45.9%)
Baseline Measures: Mean (SD)	
QOL (Q-LES-Q)	41.5 (14.2)
MDD Symptom Severity (QIDS-SR)	15.4 (5.0)

Abbreviations

QIDS-SR = Quick Inventory of Depressive Symptomatology-Self Report

Q-LES-Q = Quality of Life measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire – Short Form

Table 2

Mean and SD of Measures of depressive symptom severity (QIDS-SR), and quality of life (Q-LES-Q), with Mean (SD) of Change, and Effect Sizes or ES (Dunlap corrected)

Level*	*N*	QIDS-SR				Q-LES-Q			
		Entry Mean (SD)	Exit Mean (SD)	Change Mean (SD)	*p* (ES)	Entry Mean (SD)	Exit Mean (SD)	Change Mean (SD)	*p* (ES)
1	2,280	15.4 (4.8)	9.5 (6.5)	−6.1 (6.5)	< 0.001 (1.05)	41.5 (14.2)	56.6 (21.9)	15.1 (19.4)	< 0.001 (0.78)
2	749	14.3 (4.7)	10.5 (6.5)	−3.8 (5.8)	< 0.001 (0.65)	42.1 (15.5)	51.5 (20.1)	9.5 (17.5)	0.001 (0.52)
3	190	15.5 (4.8)	13.1 (6.3)	−2.4 (5.6)	< 0.001 (0.42)	38.8 (14.7)	42.2 (18.1)	3.4 (15.2)	0.002 (0.20)
4	56	16.4 (4.6)	12.3 (6.5)	−4.1 (6.3)	< 0.001 (0.71)	36.8 (14.3)	44.0 (19.4)	7.2 (15.6)	0.001 (0.41)
12-m. f/u	414	5.6 (3.7)	7.7 (5.7)	2.2 (5.1)	< 0.001 (0.43)	67.1 (17.8)	59.7 (20.6)	−7.4 (16.1)	< 0.001 (−0.38)

P values are considered significant at 0.01 or less (Bonferroni-adjusted), Effect sizes are Dunlap corrected for correlated designs (Dunlap et al., 1996).

*Values compared between entry and exit at each level and between entry to follow-up and exit at 12 months of f/u.

STAR*D Levels:
Level 1: Citalopram monotherapy
Level 2: Switching to sertraline, bupropion SR, venlafaxine XR, or CBT OR Augmenting with bupropion SR, buspirone, or CBT
Level 3: Switching to nortriptyline or mirtazapine OR Augmenting with lithium or T3
Level 4: Switching to tranylcypromine OR Switching to venlafaxine XR + mirtazapine

Abbreviations: QIDS-SR = Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q = Quality of Life measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire – Short Form

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Table 3

Proportions of Patients scoring at 'Within-Normal' and 'Severely-Impaired' Quality of Life at Entry and Exit from each Level and F/U.

Level*	*N*	'Within-Normal QOL'			'Severely Impaired' QOL		
		Entry (%)	Exit (%)	McNemar Tes *p* value	Entry (%)	Exit (%)	McNemar Test *p* value
1	2,280	1.7	29.1	< 0.001	85.6	50.5	< 0.001
2	749	2.9	19.5	< 0.001	83.3	59.5	< 0.001
3	190	1.6	7.9	0.008	89.5	81.1	0.023
4	56	1.8	8.9	0.220	91.1	69.6	0.004
12-m. f/u	414	46.6	31.6	< 0.001	28.5	42.5	< 0.001

P values are considered significant at 0.01 or less (Bonferroni-adjusted).

*Values compared between entry and exit at each level and between entry to follow-up and exit at 12 months of f/u.

QOL 'Within-Normal' is defined as Q-LES-Q scores within 10% of community norms. Since community norm samples have an average Q-LES-Q of 78.3 (SD=11.3), a Q-LES-Q>=70.47 is considered 'within-normal' (Endicott et al., 1993, Rapaport et al., 2005, and Schechter et al., 2007). Severe Impairment in QOL is defined as Q-LES-Q scores greater than 2 SD below the community norms. Since community norm samples have an average Q-LES-Q of 78.3 (SD=11.3), a Q-LES-Q=<55.7 is considered 'severely-impaired' (Endicott et al., 1993, Rapaport et al., 2005, and Schechter et al., 2007).

STAR*D Levels:
Level 1: Citalopram monotherapy
Level 2: Switching to sertraline, bupropion SR, venlafaxine XR, or CBT OR Augmenting with bupropion SR, buspirone, or CBT
Level 3: Switching to nortriptyline or mirtazapine OR Augmenting with lithium or T3
Level 4: Switching to tranylcypromine OR Switching to venlafaxine XR + mirtazapine

Abbreviations: Q-LES-Q = Quality of Life measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire – Short Form

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Table 4

Proportions of Remitters/Non-Remitters at 'Within-Normal and 'Severely Impaired' Quality of Life at Entry/Exit from each Level and Follow-up.

	Remitters				Non-Remitters				Difference at Exit
Level	***N***	**'Within-Normal' QOL Entry (%)**	**'Within-Normal' QOL Exit (%)**	**McNemar Test *p* value**	***N***	**'Within-Normal' QOL Entry (%)**	**'Within-Normal' QOL Exit (%)**	**McNemar Test *p* value**	**Chi-Square or Fisher Test p value**
1	812	3.0	68.0	< 0.001	1,468	1.0	7.6	< 0.001	< 0.001
2	208	5.8	52.4	< 0.001	541	1.8	6.8	< 0.001	< 0.001
3	30	0	40.0	< 0.001	160	1.9	1.9	n/a	< 0.001*
4	8	0	25.0	0.500	48	2.1	6.3	0.630	0.144*
12-mo. f/u	193	63.4	58.8	0.260	221	31.8	7.7	< 0.001	< 0.001
Level	***N***	**'Severely-Impaired' QOL Base (%)**	**'Severely-Impaired' QOL Exit (%)**	**McNemar Test *p* value**	***N***	**'Severely-Impaired' QOL Base (%)**	**'Severely-Impaired' QOL Exit (%)**	**McNemar Test *p* value**	**Chi-Square or Fisher Test p value**
1	812	79.3	9.0	< 0.001	1,468	89.0	73.4	< 0.001	< 0.001
2	208	74.5	16.3	< 0.001	541	86.7	76.2	< 0.001	< 0.001
3	30	83.3	43.3	0.004	160	90.6	88.1	0.570	< 0.001*
4	8	87.5	25	0.063	48	91.7	77.1	0.065	0.007*
12-mo. f/u	193	14.4	13.4	0.860	221	40.9	68.2	< 0.001	< 0.001

P values are considered significant at 0.01 or less (Bonferroni-adjusted).

*Fisher exact test used due to small sample size

QOL 'Within-Normal' is defined as Q-LES-Q scores within 10% of community norms. Since community norm samples have an average Q-LES-Q of 78.3 (SD=11.3), a Q-LES-Q>=70.47 is considered 'within-normal' (Endicott et al., 1993, Rapaport et al., 2005, and Schechter et al., 2007). Severe Impairment in QOL is defined as Q-LES-Q scores greater than 2 SD below the community norms. Since community norm samples have an average Q-LES-Q of 78.3 (SD=11.3), a Q-LES-Q=<55.7 is considered 'severely-impaired' (Endicott et al., 1993, Rapaport et al., 2005, and Schechter et al., 2007).

STAR*D Levels:
Level 1: Citalopram monotherapy
Level 2: Switching to sertraline, bupropion SR, venlafaxine XR, or CBT OR Augmenting with bupropion SR, buspirone, or CBT
Level 3: Switching to nortriptyline or mirtazapine OR Augmenting with lithium or T3
Level 4: Switching to tranylcypromine OR Switching to venlafaxine XR + mirtazapine

Abbreviations: f/u = Follow-up; Q-LES-Q = Quality of Life measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire – Short Form

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Impact of depression on quality-adjusted life expectancy (QALE) directly as well as indirectly through suicide

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Abstract

Purpose—To estimate quality-adjusted life expectancy (QALE) loss among US adults due to depression and QALE losses associated with the increased risk of suicide attributable to depression.

Method—We ascertained depressive symptoms using the eight-item Patient Health Questionnaire (PHQ-8) on the 2006, 2008, and 2010 Behavioral Risk Factor Surveillance System (BRFSS) surveys. We estimated health-related quality of life (HRQOL) scores from BRFSS data (n = 276,442) and constructed life tables from US Compressed Mortality Files to calculate QALE by depression status. QALE loss due to depression is the difference in QALE between depressed and non-depressed adults. QALE loss associated with suicide deaths is the difference between QALE from only those deaths that did not have suicide recorded on the death certificate and QALE from all deaths including those with a suicide recorded on the death certificate.

Results—At age 18, QALE was 28.0 more years for depressed adults and 56.8 more years for non-depressed adults, a 28.9-year QALE loss due to depression. For depressed adults, only 0.41 years of QALE loss resulted from deaths by suicide, and only 0.26 years of this loss could be attributed to depression.

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Conflict of interest The authors declare that they have no conflict of interest.

Conclusion—Depression symptoms lead to a significant burden of disease from both mortality and morbidity as assessed by QALE loss. The 28.9-year QALE loss at age 18 associated with depression markedly exceeds estimates reported elsewhere for stroke (12.4-year loss), heart disease (10.3-year loss), diabetes mellitus (11.1-year loss), hypertension (6.3-year loss), asthma (7.0-year loss), smoking (11.0-year loss), and physical inactivity (8.0-year loss).

Keywords

Depression; Suicide; Health-related quality of life (HRQOL); Quality-adjusted life expectancy (QALE); Life expectancy

Introduction

Depression can include several symptoms associated with cognition, negative affect, anxiety, and somatization and can present in individuals in various ways including brief symptoms that often resolve on their own or frequently recurring symptoms that can lead to chronic debilitating mental illness [1]. The prevalence for one kind of chronic depression, major depression, is relatively consistent across large nationally representative surveys: 6.7 % in the past 12 months and 16.6 % over a lifetime [2]. When symptoms that may indicate depression occur within the past 2 weeks, the prevalence of major depression ranges from 3.0 to 3.5 % [3]. When any such symptoms occur within the last 2 weeks, including major depression as well as episodic depression, the prevalence of depression ranges from 7 to 9 % [3].

Depression is a risk factor for many chronic conditions such as cardiovascular diseases and neurological disorders and is associated with risky behaviors such as drug, tobacco, and alcohol abuse [4–7]. Depression is also associated with poor health-related quality of life (HRQOL) and increases the number of years of life lived with disabilities [8, 9]. Depression can be life threatening and has been associated with excess mortality and substantially lower life expectancy [10, 11]. In a longitudinal study of elderly individuals followed up to 48 months, individuals diagnosed with major depression were twice as likely to die as those without depression [12]. Although this increased mortality risk may be indirectly caused by chronic conditions including diabetes and obesity and risky behaviors such as alcohol and drug use, depression alone is likely to be directly responsible through suicide for a proportion of its increased mortality risk [13, 14]. Most individuals who commit suicide have psychiatric illnesses [15]. In a systematic review of risk factors associated with suicide among depressed individuals, many of the most important risk factors included symptoms and conditions associated with depression such as more severe depression (OR = 2.20), hopelessness (2.20), anxiety (OR = 1.59), and the misuse of alcohol and drugs (OR = 2.17) [16]. In one longitudinal study, 8 % of individuals with a major depressive disorder attempted suicide over an 18-month period [17]. However, these studies have many methodological weaknesses that include less representative samples of older patients in clinical settings with multiple chronic conditions, especially those with serious mental illness [12, 17]. Estimates are lacking of the long-term health consequences and losses among representative samples of individuals with depression compared to individuals without depression across their entire life spans as well as comparisons of health losses for

those with depression compared to those with other chronic conditions. The magnitude of the impact of depression on suicide and the number of years of life lost due to the increased risk of suicide among those with depression are also unknown [13, 17].

Much of the lifetime burden of disease of depression is associated with the early age of onset of depression. In the National Comorbidity Survey (NCS), the median ages of onset for major depression, dysthymia, and bipolar disorders were 32, 31, and 25 years, respectively [2, 18], significantly younger than the ages of onset for most other chronic conditions such as heart disease and diabetes. Several different methods are available to assess the lifetime burden of disease for a condition such as the years lived with a disability (YLDs), disability-adjusted life years (DALYs), and quality-adjusted life years (QALYs) [19]. In the Global Burden of Disease Study that estimated YLDs worldwide for all infectious and chronic disease conditions, depression was the second leading cause of YLDs [8, 9]. Furthermore, when major depression is combined with other psychiatric conditions that include significant depressive symptoms (e.g., dysthymia and bipolar disorder), this combined estimate for depression is the leading health condition worldwide in terms of DALYs and YLDs [20].

QALYs and an associated measure, quality-adjusted life expectancy (QALE), take into account both the years of life lost and the relative severity of disease, making it possible to quantify the total health losses of both non-fatal and fatal mortality outcomes for affected patients or a target population [19, 21–23]. The burden of disease for non-fatal outcomes for QALYs and QALEs use preference-based HRQOL measures to assess both how a person perceives her/his health and how much that person values one health state versus another state. Preference-based HRQOL measures capture respondents' health states using a summary score anchored at 0 (dead) and 1 (perfect health) [19]. Thus, 1 year of life lived at a health state valued at 0.5 is assessed as 0.5 quality-adjusted life years (QALYs), the same as only a half year of life lived in perfect health [21, 22]. QALE at a certain age is defined and calculated as the average number of QALYs throughout the remainder of expected life [21, 22]. One advantage of QALE over DALY or YLD is that QALE uses the health state value to weight life years, so that calculating QALE loss due to depression could be useful for evaluating the economic cost of depression and for analyzing the cost-effectiveness of treatments and interventions [19, 21–23].

The first aim of this study is to estimate QALE losses due to depression for US adults and to compare such losses due to depression with previously reported losses due to five other common chronic conditions (stroke, heart disease, diabetes mellitus, hypertension, and asthma) and two significantly harmful health behaviors, smoking and physical inactivity. The second aim of this study is to estimate QALE loss due to increased risk of suicide death attributable to depression. This is the first study we are aware of to estimate QALE losses due to depression as well as losses due to increased risk of suicide death attributable to depression.

Materials and methods

We calculated QALE loss due to depression in four steps. First, using data from the Behavioral Risk Factor Surveillance System (BRFSS), we calculated HRQOL values as a function of age and depression outcome. Second, we estimated age-specific mortality rates stratified by depression status using the Compressed Mortality File. Third, using the estimated age-specific mortality rates from step 2, we constructed life tables to calculate life expectancy as a function of depression and estimate years of life lost due to depression. Fourth, we calculated QALE by combining estimated HRQOL values from step 1 and life tables from step 3. We calculated QALE by depression outcome and estimated QALE loss due to depression.

Sample

The Behavioral Risk Factor Surveillance System (BRFSS), a state-based annual health survey of non-institutionalized civilian US residents, uses random-digit-dialed telephone survey methods to ascertain sociodemographic characteristics, behavioral risk factors, and health outcomes in a population-based random sample of adults 18 years or older [24–26].

BRFSS has included the eight-item Patient Health Questionnaire (PHQ-8) depression scale as an optional module to estimate depressive symptoms and depression status during 2006, 2008, and 2010 [27]. The PHQ-8 is a valid diagnostic and severity measure for depressive disorders in large clinical studies [28] and for estimating depression prevalence [3, 27, 29]. Thirty-six States and the District of Columbia administered the PHQ-8 at least once during these three survey years, yielding a total sample size of 276,442. Current depression in this study is defined as PHQ-8 index ≥10 [27]. The PHQ-8 score of ≥10 has 88 % sensitivity and 88 % specificity for major depression and represents clinically significant depressive symptoms [4, 28, 30].

The BRFSS includes information on respondent sociodemographic characteristics, risky behaviors, and certain diseases related to current depression. We included these variables in analyses of the depression outcome to assess potential associations with these variables. The sociodemographic characteristics analyzed in this study included age, sex, race/ethnicity, marital status, and educational achievement. The risky behaviors included were weight differences from normal weight based on the body mass index (BMI)—underweight (BMI < 18.5 kg/m^2), overweight (25 ≤ BMI <30 kg/m^2), and obese (BMI ≥ 30.0 kg/m^2); current cigarette smoking (respondents who report both having smoked at least 100 cigarettes in their lifetimes and currently smoke); physical inactivity (respondents who report doing no physical activity or exercise during the past 30 days other than that for their regular job); and heavy alcohol drinking (men who report having three or more alcoholic drinks per day and women who report having two or more alcoholic drinks per day). We also assessed associations with cardiovascular-related diseases [had either a heart attack (myocardial infarction), angina or coronary heart disease, or a stroke].

Non-fatal health loss due to depression

Non-fatal health loss due to depression was defined and calculated as the decrease in HRQOL scores for those with current depression compared to those without current depression. The BRFSS questionnaire includes a set of four HRQOL questions that asks respondents to report their general health status (excellent, very good, good, fair, or poor) and the numbers of physically unhealthy days, mentally unhealthy days, and days with activity limitation during the past 30 days [31]. We applied a published mapping algorithm to obtain values of EuroQol Group's EQ-5D index, a preference-based HRQOL measurement, from the four BRFSS HRQOL items [32, 33]. This algorithm provides valid estimates of EQ-5D scores with a relative bias of less than 1 % of the actual observed EQ-5D [33].

We calculated mean EQ-5D, standardized to the year 2010 US population, for those with current depression and those without current depression, and then estimated the difference in age-adjusted EQ-5D between those with current depression and those without current depression as the non-fatal health loss due to depression.

Fatal health loss due to depression

Fatal health loss due to depression was defined as years of life lost due to depression and was operationalized as the difference in life expectancy between those with current depression and those without current depression [34]. Life expectancy at a given age is the expected/average number of years of life remaining starting at that age and is calculated from age-specific mortality rates [35, 36]. The National Center for Health Statistics compiles death data for the US population from death certificates and makes these data available to the public in the Compressed Mortality File at http://wonder.cdc.gov. The US Census Bureau provides annual population estimates (accessible at www.census.gov/popest/states/asrh/). Both sets of data include age, gender, and other basic demographics, and can be used to estimate age-specific mortality rates for the US population overall, by sex, and by some race/ethnicity subgroups.

Because age-specific mortality rates stratified by depression status are not available, these rates were estimated from three variables—age-specific mortality rates of total population, the proportion of the population with depression, and the hazard ratio of death for those with depression relative to those without depression [37]. We estimated the proportion of the population with depression from the BRFSS and the hazard ratios from the 1999–2004 National Health and Nutrition Examination Survey (NHANES) data as linked to the National Death Index through December 31, 2006 (http://www.cdc.gov/nchs/data_access/data_linkage/mortality/nhanes_99_04_ linkage.htm).

QALE loss due to depression

Like life expectancy, quality-adjusted life expectancy (QALE) at a certain age is the expected/average number of quality-adjusted life years (QALYs) remaining starting at that age and is calculated from age-specific mortality rates and corresponding average HRQOL scores [23, 36]. We constructed life tables to calculate life expectancy and QALE using the age-specific mortality rates and EQ-5D scores. For each year age interval (18–24, 25–34,…,

85 +), we obtained the mortality rates (per year per person) by dividing the numbers of deaths in that age interval by the number of persons in that age interval in the population. We assumed a constant probability of death during each age interval and could thus obtain estimated years of life within the interval [35, 36]. We calculated the QALYs during each age interval by multiplying the life-years within an interval by the corresponding mean EQ-5D value. Life expectancy and QALE for those at a certain age (such as 18 years old) are the average life years and QALYs starting from this age to the last age interval, respectively.

We used the estimated age-specific mortality rates and EQ-5D scores, stratified by depression status, to construct depression-specific life tables and to calculate QALE by respondents' depression status. Similar to years of life lost due to depression, QALE loss due to depression was defined and estimated as the difference in QALE between those with current depression and those without current depression [37, 38].

QALE loss due to increased risk of suicide death

Suicide deaths are a subset of deaths from all causes. Suicide-associated QALE loss is defined as the impact on QALE due to additional deaths through suicide. This does not include losses due to non-fatal suicide attempts. We calculated this loss as the difference between the QALE from using only those deaths that did not have suicide recorded on the death certificate and the QALE from using all deaths including those with a suicide recorded. Because the risk of suicide is higher among those with depression than among those without depression, we estimated the additional QALE loss due to this increased risk of suicide death attributable to depression as the difference in the suicide-associated QALE loss between those with and those without depression.

Ethics

This analysis used de-identified data produced by federal agencies in the public domain. Data were downloaded from the Centers for Disease Control and Prevention website (ftp://cdc.gov/pub).

Results

We first report our descriptive results (Table 1). Approximately, 9.1 % of US adults were currently depressed based on responses to the PHQ-8. The prevalence of current depression was higher among adults 18–64 years old than older adults. After age adjustment, the prevalence of depression was statistically associated with sex, race/ethnicity, marital status, and education. Specifically, the prevalence of depression was higher among women than men; black non-Hispanics than other race/ethnicity groups; divorced, separated, or never married adults than married, widowed, or unmarried cohabiting adults; and adults with less education than those with more education. Current depression was also more common among those who were underweight or obese, current cigarette smokers, physically inactive, and heavy alcohol drinkers. Those who had cardiovascular diseases were more than twice (20.1 %) as likely to be currently depressed as those who did not have cardiovascular

disease (8.0 %). Nearly half (45.6 %) of adults who reported “poor” general health and 22.1 % of adults who reported “fair” general health were currently depressed.

We also observed gender differences in the magnitude of associations between some of these predictors and current depression. For example, compared to women with depression, men with depression were more likely to have cardiovascular diseases (age-adjusted OR = 1.6), to be heavy drinkers (OR = 2.1), to be current smokers (OR = 1.3), and to be divorced, separated, or never married (OR = 1.2).

We now report our analytic results (Tables 2, 3, 4). For those with depression, the age-adjusted EQ-5D index was 0.598, 0.307 points (34 %) lower than those without depression (0.905) (Table 2). Across subgroups defined by age, sex, race/ethnicity, and simultaneously by race and sex, those who were depressed had consistently lower EQ-5D scores than those who were not depressed. This adverse impact of depression on the EQ-5D index was significantly larger for those 65 years old or older (0.509 points lower) than those 18–44 years old (0.213 points lower) or those 45–64 years old (0.413 points lower); larger for men (0.327 points lower) than women (0.304 points lower); and larger for white non-Hispanics (0.337 points lower) than black non-Hispanics (0.266 points lower) and Hispanics (0.229 points lower).

The life expectancy at age 18 years was 47.3 more years for those with depression and 63.7 more years for those without depression. This 16.4-year (26 %) decrease represents the years of life lost due to depression, starting at age 18. The loss in life expectancy at age 18 for men with depression was 18.2 years, significantly more than the 15.3 years of life lost for women with depression ($p < 0.0001$). Although the decreases in EQ-5D index were larger for white non-Hispanics than for other groups, the losses in life expectancy due to depression were significantly less for white non-Hispanics (16.1 years) than for black non-Hispanics (18.5 years) and for Hispanics (18.0 years).

The lower EQ-5D and life expectancy among those with depression yield a significantly lower QALE among those with depression (Table 3). The QALE for an 18-year-old with depression, for example, was 28.0 years, 28.9 years less than that of an 18-year-old without depression (56.8 years). This represents a decrease of QALE by more than half (51 %) for those with depression. Although QALE declined with age, depression-associated QALE losses were significant at all ages. For example, an 85-year-old person with depression had a significantly lower QALE (0.9 year) than an 85-year-old person without depression (6.9 years), a 6.0-year loss in QALE. The depression-associated QALE loss at age 18 was significantly larger among men (29.6-year loss) than among women (28.6-year loss) and larger among white non-Hispanics (29.3-year loss) than among black non-Hispanics (26.8 years) and among Hispanics (26.4-year loss), though this difference between white non-Hispanics and Hispanics was not statistically significant ($p = 0.1$).

The second aim of this study estimated suicide-associated QALE loss (Table 4). For those with depression, the calculated QALE at age 18 using non-suicide mortality rates was 28.38 years, 0.41 years more than that using mortality rates including suicides (27.97 years). Thus, death by suicide contributed 0.41 years of QALE loss for those with depression. Similarly,

death by suicide contributed only 0.15 years of QALE loss for those without depression. This 0.26-year difference (0.26 = 0.41–0.15) was the additional QALE loss associated with the increased risk for suicide among those with depression. Men lost more QALE to suicide death than women did, both for those with depression and those without depression. The additional QALE loss for men with depression due to their increased risk of death through suicide was 0.55 years, more than threefold that of the 0.14-year additional loss for women with depression.

Finally, we conducted a sensitivity analysis to examine the impact of suicide misclassification within death certificates on the QALE loss due to suicide. We included all unknown accident deaths as suicide deaths (i.e., new suicides = recorded suicides + unknown accident deaths) and recalculated the QALE loss due to suicide. The new calculated value of the additional QALE loss associated with the increased risk for suicide among depressed adults increased from 0.26 years to 0.29 years of QALE loss.

Discussion

These analyses confirmed previous studies suggesting large adverse impacts of depression on both fatal and non-fatal outcomes [4, 13, 39]. The estimated burden of disease for depression for depressed individuals during their entire life span starting at age 18 was 28.9 years of QALE loss, a loss of more than half their QALE at this age. This result is consistent with previous studies that have shown a dramatic decrease in life expectancy for those with serious mental illnesses [40, 41]. This 28.9-year loss in QALE also markedly exceeds that of other chronic conditions such as stroke (12.4-year loss), heart disease (10.3-year loss), diabetes mellitus (11.1-year loss), hypertension (6.3-year loss), and asthma (7.0-year loss), and the risk factors such as smoking (11.0-year loss) and physical inactivity (8.0-year loss) reported previously (Fig. 1) [22, 37, 42]. This QALE loss also mirrors other studies concluding that depression is the top health condition worldwide in terms of disability-adjusted life years (DALYs) [20]. At least three reasons may explain this excessive QALE loss. First, the non-fatal health losses due to depression appear significantly larger than the loss due to each of the other chronic conditions mentioned previously. Major depressive disorder contributed 917 years lived with a disability (YLDs) per 100,000 persons annually, more than those of these five other chronic conditions mentioned above combined (821 YLDs per 100,000) [9]. In our study, depression decreased the EQ-5D index by 0.307 points, equivalent to a decrease in the EQ-5D index from having no chronic conditions to having between five and six chronic conditions [43] and significantly more than the 0.07–0.16 point decrease associated with any of the five other conditions and the two risky behaviors [22, 37, 42]. Second, depression affected mortality and life expectancy more than the other conditions. People with serious mental illness, which includes clinical depression, died an average of 25 years sooner than those in the general population [44]. In this study, depression decreased life expectancy at age 18 by 16.4 years, significantly more than that of the other five chronic conditions [22] and two risky behaviors [37, 42], which ranged from 3.1 years (hypertension) to 9.8 years (stroke). Third, much of the lifetime burden of disease associated with depression is based on its early age of onset. The median ages of onset for major depression (32 years), dysthymia (31 years), and bipolar disorders (25 years) are significantly younger than those for most other chronic conditions such as heart disease and

diabetes mellitus [2]. For example, about 75 % of heart disease and 84 % of stroke occur first after age 55 [22]. In this study, the depression prevalence was significantly higher among younger persons (9.8 % for those < 65 years) than older persons (5.3 % for those ≥65 years).

Although age-adjusted depression prevalence rates in women exceeded those in men, the QALE losses associated with depression were one year more in men than in women. This difference in QALE losses between men and women resulted from the difference in the impacts on both fatal and nonfatal outcomes. Men lost significantly more years of life and experienced larger EQ-5D losses to depression than women. Compared to women with depression, men with depression were more likely to have cardiovascular diseases, to be heavy drinkers, to be current smokers, and to be divorced, separated, or never married. All of these factors are associated with poor health outcomes. Depression also has a much large impact on mortality among men than women [13, 45, 46]. Among three race/ ethnicity subgroups in our study, depression decreased the EQ-5D index more but decreased life expectancy less in white non-Hispanics than in black non-Hispanics and Hispanics, though the combined QALE loss among white non-Hispanics (28.6-year loss) significantly exceeded that among black non-Hispanics (25.8-year loss).

Our descriptive analyses of depression confirmed previous studies of associations between depression and some sociodemographic characteristics, risky behaviors, and diseases [4–7, 13, 39]. Although these variables are potential confounders for the decreased QALE among depressed individuals, our QALE estimates were not adjusted for these factors. Therefore, the term “QALE loss due to depression” does not suggest a causal relationship. However, our estimated QALE loss due to depression markedly exceeds that of diseases associated with depression, such as heart diseases and stroke, and risky behaviors, such as smoking and physical inactivity [22, 37, 42]. In addition, our study used similar methods to these previous studies and is consistent with currently accepted methods in the literature. These findings strongly suggest that depression contributes lower QALE among individuals with depression independent of these diseases and risk factors.

Depression may be directly related to the increased risk of death through suicide [13, 14] because a large proportion of persons who committed suicide had pre-existing depression [1, 47]. Nonetheless, in this study, suicide contributed very little to QALE loss for both those with depression (0.41 years) and those without depression (0.15 years). Only 0.26 years of additional QALE losses for those with depression could be attributed to their increased risk of suicide. This 0.26 years of QALE loss was much smaller than the nearly 30 years of overall QALE loss due to depression: Only 0.9 % (1.8 % for men and 0.5 % of for women) of the depression-associated QALE loss was due to the increased risk of suicide among those with depression. This most likely results from the fact that, although many who die from suicide suffer from mental disorders [48], almost all of those individuals diagnosed with a mental disorder including those with clinical depression do not die directly from suicide but from other causes [3, 13, 49]. Only 1.4 % (2.3 % for men and 0.58 % for women) of all deaths among US adults had an underlying cause of suicide, even though suicide is the second leading cause of death among those aged 15–24 years [1, 50]. Related to this, depression usually is associated with inactivity, lethargy, and a general decline in

health practices and self-care which puts those with depression at higher risk for other chronic conditions [47]. Because the Compressed Mortality File, compiled from death certificates, might underreport suicides and misclassify some suicide deaths as unknown deaths from injuries [51, 52], this study may have underestimated the impact of suicide on QALE loss. However, our sensitivity analysis showed that even attributing all unknown deaths from injuries as suicide deaths increased the estimated additional QALE loss associated with the increased risk for suicide among those with depression only 0.03 years, from 0.26 years to 0.29 years.

This study has several weaknesses. First, the PHQ-8 is not a clinical diagnostic tool for diagnosing depression but has been used primarily as a screening instrument for estimating the prevalence of depression in the general population. This would tend to reduce the accuracy and the reliability of the population estimates relative to a clinical diagnosis or interview. Second, the reporting of depressive symptoms might show mode effects that may have affected our estimates; individuals administered face-to-face interviews tend to report better health (social desirability effects) than those interviewed by telephone [3, 53]. The estimated prevalence of current depression using the BRFSS, a telephone survey, was higher (9.1 %) than the estimates using the NHANES, an in-person interview (6.8 %) [3]. However, such a higher estimated prevalence for depression would have resulted in a relatively small change in the estimated depression-associated QALE loss. For example, if we had used the estimated depression prevalence from the NHANES (6.8 % overall), the estimated QALE loss due to depression would be 28.6 years, only 0.23 year less than the 28.9 years of the estimated QALE loss based on the estimated 9.1 % overall depression prevalence from the BRFSS. Third, the BRFSS data are collected via telephone interviews using a random-digit-dialed methodology that most likely underestimates the prevalence of depression because the study population includes only non-institutionalized household members. However, our analysis demonstrates that underestimating depression prevalence would have a small effect on the estimation of QALE loss due to depression. Fourth, our estimated hazard ratios from the NHANES linked mortality data exceed others reported in the literature [12, 45], and using larger estimates of these hazard ratios would overestimate depression-associated QALE losses. If we had used the smaller estimated hazard ratio by Sullivan et al. [12] and Zheng et al. [45], the estimated QALE losses would be 26.2 years (28.1 years for men and 25.0 years for women). However, such estimates were not statistically significantly different from the estimated QALE losses in this study. Fifth, this study relies on the BRFSS's unhealthy days questions to estimate preference-based HRQOL scores indirectly rather than on direct measurements of these scores. Therefore, our estimates of QALE loss are likely to be smaller than the true values due to "regression to the mean" [32–37]. One study estimated the bias of estimated QALE loss using the estimated EQ-5D scores and found that this bias was less than 2.5 % of that using the actual EQ-5D questions [36]. Finally, not all the US states used the PHQ-8 questionnaire. Thus, if the prevalence of depression in the states using this questionnaire differed from that in the states not using this questionnaire, these results may not be fully generalizable to the entire US population. However, our analysis above on the small effects of differences in estimated depression prevalence on QALE loss due to depression may mitigate this lack of generalizability.

This study is the first we know of to estimate burden of disease for depression by comparing the QALE for currently depressed persons to that for non-depressed persons. QALE is a single index that encompasses both depression-related fatal and nonfatal outcomes. Therefore, our results are particularly useful in directly comparing the burdens of disease for depression to the burdens of disease for other chronic conditions and risky behaviors and for estimating the economic costs of depression among U.S adults [19–23]. The overall burden of depression was at least twice as large as the burdens of some common chronic conditions such as stroke, heart disease, diabetes mellitus, hypertension, and asthma and of the risk factor of smoking. This information could be useful to local and state authorities when setting health priorities and when dealing with mental problems in the general adult population [54, 55]. These results will also likely to motivate the development of improved prevention efforts and strategies for individuals at risk for depression and suicide [56–58].

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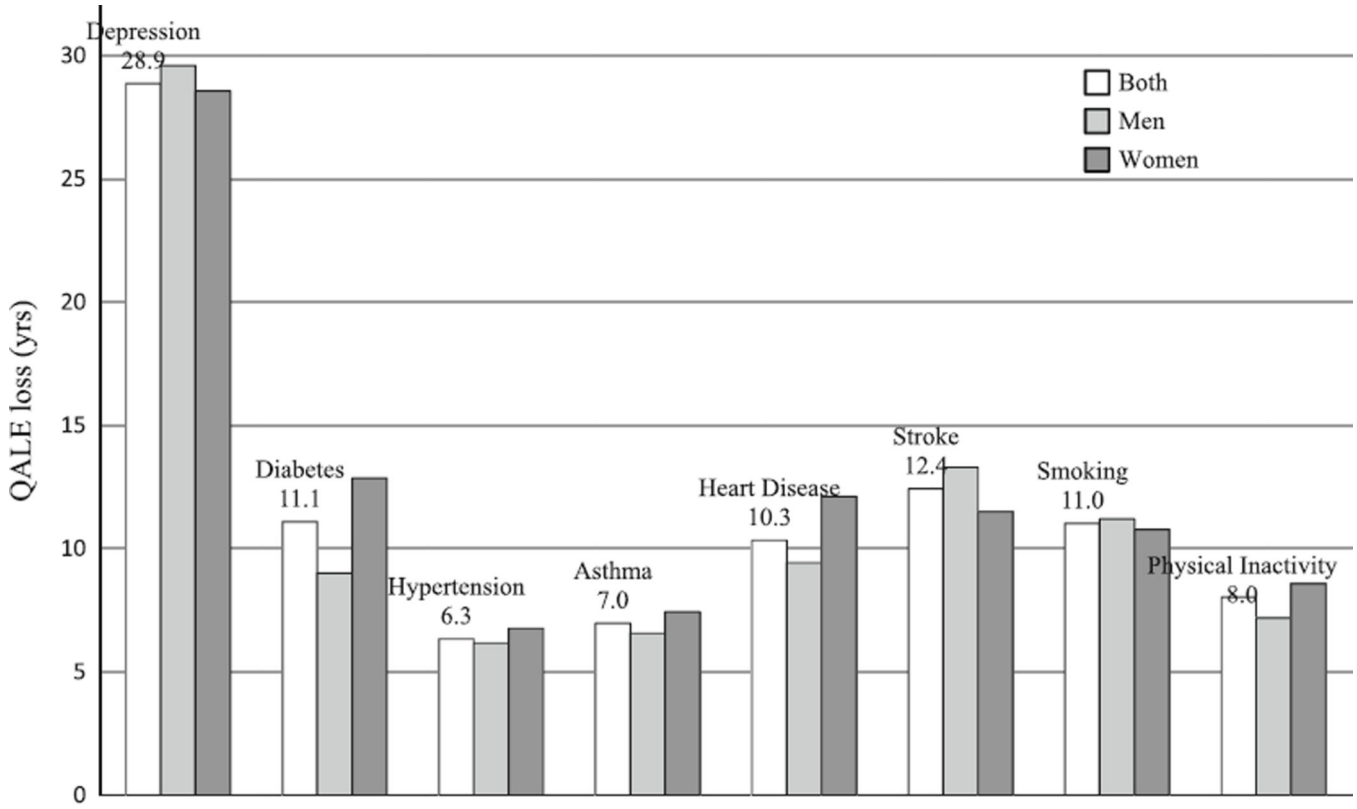

Fig. 1.

Comparison of quality-adjusted life expectancy (QALE) losses due to depression, diabetes mellitus [22], hypertension [22], asthma [22], heart disease [22], stroke [22], smoking [37], and physical inactivity [42]

Table 1

Proportions of Current Depression among US adults by various characteristics

Characteristics	Proportion of current depression		
	N	Percentage[a]	SE (%)
All	276,442	9.1	0.13
Age			
18–44	85,974	9.6	0.21
45–64	116,716	10.0	0.20
65+	73,752	5.3	0.17
Sex			
Men	105,354	7.1	0.44
Women	171,080	11.0	0.44
Race/ethnicity			
White non-Hispanics	217,215	8.6	0.43
Black non-Hispanics	26,234	11.8	0.54
Hispanics	14,505	9.4	0.65
Others	16,526	8.7	0.65
Marital status			
Married/widowed/unmarried couples	196,679	7.2	0.44
Divorced/separated/never married	79,057	13.5	0.46
Education			
<High School	25,306	17.2	0.73
High school/some college	158,346	10.1	0.44
College graduate	92,485	4.6	0.41
Body mass index (BMI) category, (kg/m^2)			
<18.5 (underweight)	4,476	13.4	1.23
18.5 to <25 (normal weight)	93,014	7.4	0.45
25 to <30 (overweight)	96,844	7.6	0.45
≥30 (obese)	72,421	13.2	0.48
Current smoking			
Yes	50,206	17.9	0.54
No	225,337	6.9	0.41
Physical activity			
Yes	207,032	6.6	0.41
No	69,215	17.1	0.56
Heavy alcohol drinking			
Yes	13,443	12.6	0.85
No	258,662	8.9	0.42
Cardiovascular diseases			
Yes	30,246	20.1	0.75
No	244,031	8.0	0.43

Characteristics	Proportion of current depression		
	N	Percentage[a]	SE (%)
Self-rated general health			
Excellent	52,535	2.2	0.43
Very Good	90,222	4.1	0.42
Good	83,350	9.5	0.53
Fair	34,696	22.1	0.72
Poor	14,869	45.6	1.06

SE standard error of estimate

[a]Weighted proportions of depression, for subgroups except age group itself, proportions were adjusted by age

Table 2

Impact of depression on EQ-5D scores and life expectancy (LE)

Characteristics	Not depression		Depression		Difference		Not depression		Depression		Difference	
	HRQOL[a]	SE	HRQOL[a]	SE	Loss[b]	SE	LE at age 18[c]	SE	LE at age 18[d]	SE	LE Loss at age 18[d]	SE
All	0.905	0.001	0.598	0.005	0.307	0.005	63.7	0.05	47.3	0.05	16.4	0.06
By age												
18–44	0.934	0.001	0.721	0.006	0.213	0.006	63.7	0.05	47.3	0.05	16.4	0.06
45–64	0.892	0.001	0.479	0.008	0.413	0.008	38.0	0.05	24.0	0.04	14.0	0.06
65+	0.838	0.002	0.330	0.013	0.509	0.014	20.8	0.05	10.5	0.03	10.3	0.05
By sex												
Men	0.912	0.002	0.585	0.009	0.327	0.010	61.2	0.08	43.0	0.07	18.2	0.10
Women	0.899	0.003	0.595	0.006	0.304	0.006	66.1	0.08	50.8	0.12	15.3	0.17
By race/ethnicity												
White non-Hispanics	0.910	0.003	0.572	0.006	0.337	0.007	63.5	0.05	47.4	0.05	16.1	0.06
Black non-Hispanics	0.894	0.003	0.627	0.011	0.266	0.011	61.1	0.22	42.6	0.10	18.5	0.21
Hispanics	0.890	0.003	0.661	0.015	0.229	0.015	69.2	0.49	51.2	0.18	18.0	0.46
By sex and race/ethnicity												
White non-Hispanic men	0.917	0.003	0.571	0.010	0.346	0.011	61.1	0.08	43.2	0.07	17.9	0.10
White non-Hispanic women	0.903	0.003	0.573	0.007	0.330	0.008	65.8	0.08	50.8	0.12	15.0	0.17
Black non-Hispanic men	0.898	0.002	0.637	0.024	0.261	0.024	57.4	0.27	37.5	0.21	19.9	0.25
Black non-Hispanic women	0.890	0.003	0.623	0.011	0.268	0.011	64.5	0.39	46.6	0.25	18.0	0.52
Hispanic men	0.899	0.004	0.661	0.030	0.238	0.030	66.7	0.60	46.6	0.32	20.1	0.55
Hispanic women	0.882	0.004	0.662	0.015	0.220	0.016	71.7	0.89	54.8	0.52	16.9	1.10

SE standard error of estimate

[a] EQ-5D index, for subgroups except age group itself, age-adjusted EQ-5D index

[b] Decrease in EQ-5D index for those with depression

[c] Life expectancy at age 18 years. For the three ages, life expectancy at age 18, 45, and 65 years, respectively

[d] Life expectancy loss due to depression at age 18 years. For the three ages, life expectancy loss at age 18, 45, and 65 years, respectively

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Table 3

Impact of depression on quality-adjusted life expectancy (QALE)

Characteristics	Not depression		Depression		Difference	
	QALE at age 18[a]	SE	QALE at age 18[a]	SE	QALE loss at age 18[b]	SE
All	56.8	0.08	28.0	0.19	28.9	0.21
At ages						
At 18	56.8	0.08	28.0	0.2	28.9	0.21
At 25	50.5	0.08	22.7	0.2	27.8	0.20
At 35	41.5	0.08	16.1	0.2	25.4	0.19
At 45	32.8	0.08	10.4	0.2	22.3	0.17
At 55	24.7	0.08	6.6	0.1	18.1	0.17
At 65	17.3	0.08	3.5	0.1	13.8	0.17
At 75	11.2	0.10	1.8	0.1	9.4	0.16
At 85	6.9	0.14	0.9	0.1	6.0	0.15
By sex						
Men	55.2	0.10	25.6	0.33	29.6	0.35
Women	58.4	0.14	29.8	0.24	28.6	0.28
By race/ethnicity						
White non-Hispanics	56.9	0.07	27.6	0.23	29.3	0.24
Black non-Hispanics	53.7	0.27	26.9	0.37	26.8	0.46
Hispanics	58.0	1.58	31.6	0.87	26.4	1.76
By sex and race/ethnicity						
White non-Hispanic men	55.4	0.09	25.6	0.37	29.7	0.38
White non-Hispanic women	58.4	0.10	29.2	0.28	29.2	0.30
Black non-Hispanic men	51.0	0.35	24.9	0.66	26.0	0.72
Black non-Hispanic women	56.2	0.41	28.6	0.45	27.6	0.63
Hispanic men	59.1	0.84	28.2	1.25	30.8	1.48
Hispanic women	57.9	2.36	34.2	1.13	23.7	2.58

SE Standard error of estimate

[a]QALE at age 18 years. For the eight ages, QALE at age 18, 25, 35, 45, 55, 65, 75, and 85 years, respectively

[b]QALE loss due to depression at age 18 years. For the eight ages, QALE loss at age 18, 25, 35, 45, 55, 65, 75, and 85 years, respectively

Table 4

Additional quality-adjusted life expectancy (QALE) loss associated with the increased risk of suicide attributable to depression

Sex	Depression	Use all-cause mortality		Use non-suicide mortality		Loss to suicide	
		QALE[a]	SE	QALE[a]	SE	Loss[b]	SE
Both	Yes	27.97	0.19	28.38	0.20	0.41	0.01
	No	56.84	0.08	56.99	0.08	0.15	0.01
				Additional loss[c]		0.26	0.01
Men	Yes	25.64	0.33	26.40	0.35	0.76	0.03
	No	55.24	0.10	55.45	0.10	0.21	0.01
				Additional loss[c]		0.55	0.03
Women	Yes	29.80	0.24	30.02	0.24	0.22	0.02
	No	58.38	0.14	58.46	0.14	0.08	0.02
				Additional loss[c]		0.14	0.02

SE standard error of estimate

[a] Calculated QALE at age

[b] QALE loss at age 18 due to additional deaths by suicide

[c] Additional QALE loss at age 18 due to increased risk of suicide among those with depression

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Describing the population health burden of depression: health-adjusted life expectancy by depression status in Canada

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Abstract

Introduction: Few studies have evaluated the impact of depression in terms of losses to both premature mortality and health-related quality of life (HRQOL) on the overall population. Health-adjusted life expectancy (HALE) is a summary measure of population health that combines both morbidity and mortality into a single summary statistic that describes the current health status of a population.

Methods: We estimated HALE for the Canadian adult population according to depression status. National Population Health Survey (NPHS) participants 20 years and older (n = 12 373) were followed for mortality outcomes from 1994 to 2009, based on depression status. Depression was defined as having likely experienced a major depressive episode in the previous year as measured by the Composite International Diagnostic Interview Short Form. Life expectancy was estimated by building period abridged life tables by sex and depression status using the relative risks of mortality from the NPHS and mortality data from the Canadian Chronic Disease Surveillance System (2007–2009). The Canadian Community Health Survey (2009/10) provided estimates of depression prevalence and Health Utilities Index as a measure of HRQOL. Using the combined mortality, depression prevalence and HRQOL estimates, HALE was estimated for the adult population according to depression status and by sex.

Results: For the population of women with a recent major depressive episode, HALE at 20 years of age was 42.0 years (95% CI: 40.2–43.8) compared to 57.0 years (95% CI: 56.8–57.2) for women without a recent major depressive episode. For the population of Canadian men, HALE at 20 was 39.0 years (95% CI: 36.5–41.5) for those with a recent major depressive episode compared to 53.8 years (95% CI: 53.6–54.0) for those without. For the 15.0-year difference in HALE between women with and without depression, 12.3 years can be attributed to the HRQOL gap and the remaining 2.7 years to the mortality gap. The 14.8 fewer years of HALE observed for men with depression equated to a 13.0-year HRQOL gap and a 1.8-year mortality gap.

Conclusion: The population of adult men and women with depression in Canada had substantially lower healthy life expectancy than those without depression. Much of this gap is explained by lower levels of HRQOL, but premature mortality also plays a role.

Keywords: *life expectancy, healthy life expectancy, mortality, health-related quality of life, depression*

Highlights

- Men and women in Canada who have depression live a substantially higher proportion of their life in an unhealthy state compared to their counterparts without depression.
- This gap in healthy life expectancy between Canadians with and without depression is primarily associated with losses in quality of life.
- Emotional state, cognitive state and pain are the key attributes associated with losses in quality of life for Canadians experiencing a recent major depressive episode.
- Based on observations from past studies of the Canadian household population, the burden of depression on healthy life expectancy at a population level appears to be greater than that associated with other chronic conditions such as diabetes, hypertension and obesity.

Introduction

Depression contributes significantly to the burden of disease throughout the world, including in Canada.[1] It is estimated that over 298 million people worldwide are living with depression.[2] In 2012, about 3.2 million Canadians over the age of 15 (11.3%) reported having experienced symptoms consistent with a major depressive episode in their lifetime, while the prevalence of such an episode in the previous 12 months was 4.7% in this population.[3] Women and young people aged 15 to 24 years experienced the highest prevalence of a 12-month major depressive episode.[3]

Depression has an important impact on health-related quality of life (HRQOL), functioning, mortality due to intentional injury and health care utilization.[4-6] In

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addition to these direct negative outcomes, depression has also been demonstrated to increase risk for coronary heart disease,[7] stroke[8] and cancer[9] and a decline in physical functioning.[10] Potential mechanisms for the relationship between depression and physical disease include immune and endocrine dysregulation and inflammatory processes.[11] Depression has also been associated with an increased risk of mortality in general community populations, as well as in patient populations with chronic illnesses such as coronary heart disease, cancer, diabetes and stroke.[11] There are likely reciprocal effects between depression and disease, with depression being a risk factor for, and a sequela of, disease.[11]

Summary measures of population health using the Global Burden of Disease methodology[1,12–15] have ranked depression very high on the list of health conditions contributing to the global and national burden of disease, particularly in terms of losses due to disability. Major depressive episode is the second leading cause of years lived with disability globally[1] as well as in the United States,[12] the United Kingdom,[13] China[14] and Canada.[15]

Less well documented is the association of depression with life expectancy and healthy (or disease-free) life expectancy. Understanding both life expectancy and healthy life expectancy among people who have depression will help to better characterize its disease burden. A recent systematic review and meta-analysis[16] concluded that people living with a mood disorder have a mortality rate twice as high as those without a mood disorder, and potential years of life lost due to mental disorders ranged from 1.4 to 32 years, with a median of 10.1 years. Jia et al.[17] reported that adults living with depression in the United States experienced a 28.9 year loss of quality adjusted life expectancy (QALE) at age 18 compared to those without depression. Results from the few existing studies on healthy or disease-free life expectancy and depression are not consistent.[18-20] A number of these studies are restricted to older adults and thus cannot be generalized to the entire population. These studies also use a measure of functional health restricted to activities of daily living, which do not consider attributes such as pain, emotion and cognition.

The objective of our study was to estimate period life expectancy (LE) and health-adjusted life expectancy (HALE) of Canadian adults (aged 20 years and older) according to depression status. Note that the period approach to estimating LE and HALE adopted in this paper is a summary measure of population health for a given period. Period life expectancy estimates the hypothetical life expectancy of an individual were they to experience the age- and sex-specific mortality rates in a given period. This should not be confused with projected life expectancy based on modelling or cohort life expectancy based on the actual mortality experience of a specific cohort. In a similar fashion, period HALE is a hypothetical estimate reflecting an individual's healthy life expectancy were they to experience the age- and sex-specific mortality and age- and sex-specific HRQOL levels at a given point in time.

These estimates are useful to better understand the population health impact of a condition. They are also useful for informing policy and programs, and for making decisions about the relative burden of specific health conditions. Because of the varied course of depression, with both chronic and episodic cases included in the population studied, the estimates in this study should not be applied to predict the expected health course of any individual.

Methods

Data sources

To estimate HALE, several types of data are necessary: all-cause mortality rates by depression status, depression prevalence and HRQOL estimates by depression status. All-cause mortality rates for the Canadian adult population with and without depression were estimated based on a methodology that partitions rates for total population into mortality rates by disease categories using a mortality relative risk or hazard ratios and a prevalence of those categories. The methodology is described in detail in our previous study.[21]

We used data from the following three sources:

- National Population Health Survey (NPHS), for estimating mortality hazard ratios (HRs) by depression status;
- Canadian Community Health Survey (CCHS), for estimating depression prevalence and HRQOL by depression status; and
- Canadian Chronic Disease Surveillance System (CCDSS), for actual age- and sex-specific all-cause mortality rates in the Canadian population, which were then partitioned into those associated with depression and those not associated with depression, based on the mortality HR estimated using the NPHS and depression prevalence estimated from CCHS.

The NPHS is a longitudinal survey conducted by Statistics Canada of 17 276 Canadians of all ages living in households in the 10 provinces. The NPHS has a biennial follow-up spanning the years 1994/95 to 2010/11 and includes death clearance against the Canadian Mortality Database.[22] These data were used to estimate mortality HR associated with depression required for estimating all-cause mortality rates for people with and without depression. Our study population at baseline included 12 373 participants aged 20 years and older.

The CCHS is an annual cross-sectional survey, conducted by Statistics Canada, of a sample of approximately 65 000 Canadians aged 12 years and older living in households in the provinces and territories.[23] Our study used a two-year CCHS sample (2009–2010) and included 103 815 participants aged 20 years and older. We used these data to estimate the prevalence of depression, as well as to attribute depression status in estimating all-cause mortality rates (see "Analysis" section for more detail). We also obtained Health Utilities Index (HUI) scores by depression status from the CCHS. We estimated depression prevalence and HUI scores from the CCHS because the data were more recent, and the larger sample size allowed for more accurate estimation of depression and HUI scores.

We used CCDSS all-cause mortality data for the period of 2007–2009 in the study. The CCDSS collects administrative data that include death and population counts by sex and five-year age groups for all residents of all ages in all provinces and territories, who use the public health care systems. Both mortality and population size information come from provincial and territorial health insurance databases

that cover about 97% of the Canadian population. Data are collected from all Canadian provinces and territories and summarized by the Public Health Agency of Canada.[24]

Measures

Depression is measured in the CCHS and NPHS using the Composite International Diagnostic Interview Short Form (CIDI-SF) instrument. The CIDI is a structured diagnostic interview, based on diagnostic criteria from the *International Classification of Diseases (ICD-10)* and the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*, that is administered by trained interviewers. The short form of the Interview is based on a subset of CIDI questions that could still reliably reproduce prevalence estimates.[25] The CIDI-SF interview produces scores that give predicted probabilities of depression. For this study, respondents with a predicted probability of 0.9 and above were considered to have experienced a major depressive episode during the previous year. The CIDI-SF was optional content on the 2009–2010 CCHS, and not all provinces and territories chose to include this module. Estimates of depression are based on partial provincial and territorial coverage that includes five provinces (Prince Edward Island, Quebec, Saskatchewan, Alberta and British Columbia) and two territories (Nunavut and Northwest Territories).

HRQOL is measured using the Health Utilities Index Mark 3 instrument in the CCHS. The HUI is a preference-based measure of HRQOL based on responses to questions about functioning for the following eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain.[26] Single-attribute utility scores range from 0.0 (lowest level of functioning) to 1.0 (full functional capacity). The eight attributes are combined into an overall score that ranges from 1.00 (perfect health) through 0.00 (death) to −0.36 (the worst possible health state; from a preference perspective, some health states are considered worse than death and are consequently assigned negative scores). A change of 0.03 or more in overall HUI scores and 0.05 or more in single-attribute utility scores is considered clinically important.[27]

The HUI has been widely used, and its validity and reliability in a variety of applications is supported.[27,28] A study assessing the sensitivity to depression outcomes of several multiattribute utility indexes found HUI to be able to discriminate well between levels of severity in the two depression instruments being evaluated.[29] The HUI score is used as a morbidity measure in the estimation of HALE. Depression typically has a negative impact on the emotional state, including sustained negative affect and difficulties experiencing positive affect.[30] In order to assess whether HRQOL differences are due exclusively to changes in the HUI emotion attribute, we compared HUI scores (all ages combined) by depression status for each of the eight attributes.

Analysis

Relative risks of mortality by depression status for women and for men were approximated by HRs. The HRs were estimated by fitting sex-specific discrete-time proportional models with a complementary log-log function using the completed NPHS data. We defined people with depression as those with a high probability (0.9) of having had a major depressive episode in the 12 months prior to data collection in at least one NPHS cycle, according to a method described by Simpson et al.[31] The first episode defined a case date. Respondents were followed up for mortality events every two years and a variable for each cycle was included in the model (cycle 1–cycle 9) as a time-interval measure. The sex-specific models were adjusted by age. As the HRs were used to estimate only all-cause mortality rates associated with depression, we did not adjust the models for any other comorbidities, socioeconomic status or other determinants of health. Because of the complex sample design of this survey, we used the bootstrapping method to calculate variance and produce 95% confidence intervals (CIs) for HR.[22] Age- and sex-specific depression prevalences, required for decomposing total mortality rates by depression status, were estimated using the CCHS 2009–2010. Mean HUI estimates by age, sex and depression status were also calculated. Bootstrapping was used to generate 95% CI.[23] In our study, total mortality rates by sex and 5-year age groups were estimated from CCDSS data for the period of 2007–2009. In this study, age- and sex-specific mortality rates for people with depression and for those without depression were estimated by decomposing mortality rates for the total population following the methodology we described in our previous study.[21]

We used the Chiang method[32] to generate period (2007–2009) sex-specific abridged life tables by depression using 14 standard age groups (20–24, 25–29, …, 80–84, ≥ 85 years). The Gompertz function was used to provide an accurate estimate of LE for the last open-ended 85-years-plus age interval in order to close the life table, as described by Hsieh.[33] The modified Sullivan method[34] was used for HALE estimation. According to this method the "life-years lived" was adjusted by the HUI.

$$L_x^{'} = L_x * HUI_x$$

where $L_x^{'}$ is adjusted life-years lived in age-interval x, L_x is life-years lived in age-interval x and HUI_x is Health Utilities Index Mark 3 for people in age-interval x.

The variance of LE and HALE was estimated using bootstrap methodology. Statistics Canada's surveys provide 500 bootstrap weights for variance estimation to account for complex survey designs.[22,23] Using those weights, 500 sets of HR estimates from NPHS and 500 sets of prevalence of depression and HUI estimates from CCHS were generated and all unique combinations of those estimates used to obtain mortality rates to build 250 000 life tables by depression and sex. This allowed estimating LE and HALE variance, building CIs around point estimates and conducting z tests to determine the statistical significance of the differences in LE and HALE. The 95% CIs were built based on the normality assumption. Due to the nature of the study population (adults 20 years and older), LE and HALE results were estimated at age 20 years and not birth.

The Arriaga decomposition, or partitioning, method[35] (adapted for the Sullivan method[34]) was applied to quantify which part of HALE differences according to depression status can be attributable to differences in premature mortality and which are attributable to loss of HRQOL (morbidity). For each age group, the change in HALE between the comparison groups is partitioned into the following components:

$$\Delta HALE = \Delta MORB + \Delta MORT = \frac{L_{x1} + L_{x2}}{2} \Delta HUI + \frac{HUI_1 + HUI_2}{2} \Delta L_x$$

where $\Delta MORB$ estimates change due to HRQOL, $\Delta MORT$ estimates change due to mortality, L_{x1} and HUI_{x1} refer to the number of years lived and HUI score respectively for those with depression for age-interval x, and L_{x2} and HUI_{x2} refer to the number of years lived and HUI score respectively for those without depression for age-interval x. (More details about how this methodology is applied to healthy life expectancy estimations can be found elsewhere.[21,36])

Results

Table 1 shows the demographic characteristics of the participants in the NPHS and CCHS, the two national health surveys that we used for this study. The prevalence of major depressive episode in our study population (2009/10) was 5.5% (6.7% for women and 4.2% for men; results not shown).

Based on analysis of the NPHS data, there were 2154 deaths over the 16-year follow-up period. Mortality risk was significantly higher for those who experienced a major depressive episode (age-adjusted HR = 1.43; 95% CI: 1.22–1.68). This significant risk persisted when we restricted analyses to women only (age-adjusted HR = 1.55; 95% CI: 1.28–1.87), while the risk for men was nonsignificant (age-adjusted HR = 1.28; 95% CI: 0.98–1.68) (data not shown).

Unadjusted HRQOL values (as measured by HUI scores) varied by age, sex and depression status (see Table 2). HUI scores were considerably lower in all age groups for men and women who had experienced a major depressive episode during the preceding 12 months compared to those who had not experienced such an episode. According to definitions of disability categories based on global HUI scores developed by Feng et al.,[37] men and women with depression experienced on average moderate disability (HUI < 0.89) at all age groups, whereas only older (≥ 55 years) men and women without depression fell into this category. Similarly, men with depression on average experienced severe disability (HUI < 0.70) at age 40 years while women experienced this at age 45 years; average HUI scores for men and women without depression did not drop below this threshold at any age group in our study.

An assessment of each of the eight HUI attributes by sex (all ages combined) showed that depression was associated with a clinically meaningful lower score (i.e. a difference of 0.05 or higher) for the emotion, pain and cognition attributes (Table 2).

Both LE and HALE for women with depression were lower than for those without depression; LE for men with depression was not significantly lower whereas HALE was (Table 3). LE at age 20 was 4.1 years (95% CI: 1.1–7.1) lower for women with depression compared to those without, whereas HALE at age 20 was 15.0 years (95% CI: 13.2–16.8) lower for women with depression. For men, the gap in LE at age 20 between those with and without depression was 2.7 years (95% CI: 0.0–5.4), whereas HALE at age 20 for men with depression was 14.8 years (95% CI: 12.3–17.4) lower. LE and HALE at age 65 were lower for both women and men with depression. Women with depression had an LE at age 65 years that was 3.2 years (95% CI: 1.8–4.6) lower and a HALE at age 65 that was 6.7 years (95% CI: 5.3–8.1) lower than women without depression. LE at age 65 years for men with depression was 2.1 years (95% CI: 0.1–4.1) lower than that of men without depression. HALE at age 65 years was 6.0 years (95% CI: 3.8–8.2) less for men with depression compared to those without depression.

An assessment of the individual contribution of loss of HRQOL and premature mortality to differences in HALE at age 20 indicated that, for the 15.0-year difference in HALE between women with and without depression, 12.3 years could be attributed to HRQOL losses and the remaining 2.7 years to mortality losses. The 14.8 fewer years of HALE for men with depression equated to a 13.0-year HRQOL gap

TABLE 1
Demographic characteristics of survey participants, NPHS 1994/95 and CCHS 2009/10

Characteristics	NPHS 1994/95	CCHS 2009/10
Age, mean (range) in years	45 (20–100)	47.5 (20–102)
Sex,[a] % (95% CI)		
Male	48.6 (48.3–48.9)	49.1 (49.1–49.1)
Female	51.4 (51.1–51.7)	50.9 (50.9–50.9)
Marital status,[b] % (95% CI)		
Married/common-law	68.3 (67.3–69.3)	65.7 (65.1–66.3)
Single/widowed/divorced/separated	31.7 (30.7–32.7)	34.3 (33.7–34.9)
Highest level of education,[c] % (95% CI)		
Less than high school	25.7 (24.5–26.8)	14.4 (14.1–14.8)
High school graduation	40.7 (39.5–41.9)	23.7 (23.3–24.2)
Post-secondary graduation	33.6 (32.5–34.8)	61.8 (61.3–62.4)
Depression,[d] % (95% CI)		
Yes	NA	5.5 (5.2–5.9)
No	NA	94.5 (94.1–94.8)
Depression[d] in at least one cycle (1994–2008), % (95% CI)		—
Yes	4.7 (4.4–4.9)	NA
No	95.3 (95.0–95.6)	NA

Abbreviations: CCHS, Canadian Community Health Survey; CIDI-SF, Composite International Diagnostic Interview Short Form; NA, not applicable; NPHS, National Population Health Survey.

[a] n = 12 373 (NPHS); n = 103 815 (CCHS).

[b] n = 12 371 (NPHS); n = 103 636 (CCHS).

[c] n = 12 347 (NPHS); n = 101 783 (CCHS).

[d] Based on responses to CIDI-SF, indicative of having experienced a major depressive disorder in the previous year. n = 3501 (NPHS); n = 48 355 (CCHS).

TABLE 2
Health-related quality of life status by sex, age, HUI attribute and depression status[a], Canada, 2009/10

	Average Health Utilities Index score (95% CI)			
	Women without depression	Women with depression	Men without depression	Men with depression
Age group (years)				
20–24	0.93 (0.92–0.94)	0.82 (0.77–0.87)	0.93 (0.92–0.94)	0.74 (0.65–0.83)
25–29	0.94 (0.93–0.95)	0.81 (0.76–0.85)	0.93 (0.92–0.94)	0.81 (0.76–0.87)
30–34	0.93 (0.93–0.94)	0.74 (0.65–0.84)	0.93 (0.92–0.94)	0.78 (0.71–0.85)
35–39	0.93 (0.92–0.94)	0.74 (0.64–0.84)	0.93 (0.92–0.94)	0.80 (0.74–0.87)
40–44	0.91 (0.90–0.92)	0.73 (0.68–0.78)	0.91 (0.89–0.92)	0.68 (0.60–0.77)
45–49	0.91 (0.89–0.92)	0.63 (0.54–0.71)	0.92 (0.90–0.93)	0.67 (0.58–0.76)
50–54	0.90 (0.89–0.91)	0.69 (0.63–0.75)	0.91 (0.90–0.91)	0.66 (0.59–0.73)
55–59	0.88 (0.87–0.89)	0.71 (0.65–0.77)	0.88 (0.87–0.89)	0.59 (0.49–0.70)
60–64	0.88 (0.87–0.89)	0.68 (0.62–0.75)	0.90 (0.89–0.91)	0.62 (0.52–0.72)
65–69	0.87 (0.86–0.88)	0.59 (0.49–0.69)	0.88 (0.87–0.89)	0.60 (0.49–0.71)
70–74	0.86 (0.85–0.88)	0.67 (0.58–0.77)	0.87 (0.85–0.88)	0.63 (0.45–0.81)
75–79	0.81 (0.78–0.83)	0.66 (0.54–0.78)	0.83 (0.81–0.85)	0.69 (0.39–1.00)
80–84	0.79 (0.77–0.82)	0.48 (0.16–0.81)	0.79 (0.76–0.82)	0.36 (−0.01–0.73)
≥ 85	0.72 (0.69–0.75)	0.52 (0.37–0.67)	0.74 (0.70–0.78)	0.44 (0.10–0.79)
HUI attribute				
Vision	0.99 (0.99–0.99)	0.99 (0.98–0.99)	0.99 (0.99–0.99)	0.99 (0.99–0.99)
Speech	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
Pain	0.97 (0.97–0.97)	0.92[b] (0.91–0.93)	0.98 (0.97–0.98)	0.93[b] (0.91–0.94)
Mobility	0.99 (0.99–0.99)	0.99 (0.98–0.99)	1.00 (1.00–1.00)	0.99 (0.98–0.99)
Hearing	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	0.99 (0.99–1.00)
Emotion	0.99 (0.99–0.99)	0.94[b] (0.93–0.95)	0.99 (0.99–0.99)	0.92[b] (0.91–0.93)
Dexterity	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
Cognition	0.98 (0.98–0.98)	0.93[b] (0.92–0.94)	0.98 (0.98–0.98)	0.93[b] (0.92–0.94)

Abbreviations: CI, confidence interval; CIDI-SF, Composite International Diagnostic Interview Short Form; HUI, Health Utilities Index.

Note: Light shading signifies moderate disability (global HUI score of 0.70–0.88); dark shading signifies severe disability (global HUI score < 0.70); no shading represents either no disability (global HUI score = 1.00) or mild disability (global HUI score = 0.89–0.99).

[a] Based on responses to CIDI-SF, indicative of having experienced a major depressive episode in the previous year.

[b] Clinically meaningful difference in attribute-specific HUI score between those with and without depression.

and a 1.8-year mortality gap (data not shown).

We found large differences between adult Canadians with and without depression in terms of the percentage of their life spent in an unhealthy state (calculated as [LE − HALE]/LE; see Figure 1). Both men and women with depression spent almost three times as much of their life expectancy at age 20 in poor health when compared to those without depression (31% vs. 12% for females and 32% vs. 11% for males). These large differences persisted across age groups: based on LE and HALE at age 65, men and women with depression were still living approximately twice as long in poor health as men and women of the same age without depression (40% vs. 19% for women and 43% vs. 17% for men).

Discussion

In this study, we found significantly lower LE at age 20 for women, and HALE at age 20 for both women and men, among Canadians reporting symptoms consistent with a major depressive episode in the previous 12 months. We found this across age groups, although gaps in the proportion of life expectancy spent in an unhealthy state were greater among men and younger age groups with depression.

Although direct comparisons with other health problems need to be interpreted with caution, we found that losses of HALE associated with depression in the Canadian adult population were larger than those observed for obesity class 2 and above,[21] and for diabetes and hypertension[38] in the same population. In addition, while those studies found a greater loss of HALE among women than men, we demonstrated approximately equal losses for both sexes.

Our results align with those of Jia et al.,[17] who reported a 28.9-year QALE loss at age 18 for adults with depression, which is substantively larger than the approximately

TABLE 3
Life expectancy and HALE at age 20–24 and at 65–69, by sex and depression status[a], Canada, 2009/10

		Years (95% CI)			
	Age group, years	Women without depression	Women with depression	Men without depression	Men with depression
Life expectancy	20–24	64.9 (64.8–65.0)	60.8 (59.0–62.6)	60.4 (60.3–60.5)	57.7 (55.0–60.4)
	65–69	22.4 (22.3–22.5)	19.2 (17.8–20.6)	19.1 (19.1–19.1)	17.0 (15.0–19.0)
Health-adjusted life expectancy	20–24	57.0 (56.8–57.2)	42.0 (40.2–43.8)	53.8 (53.6–54.0)	39.0 (36.5–41.5)
	65–69	18.1 (17.9–18.3)	11.4 (10.0–12.8)	15.8 (15.6–16.0)	9.8 (7.6–12.0)

Abbreviations: CI, confidence interval; CIDI-SF, Composite International Diagnostic Interview Short Form; HALE, health-adjusted life expectancy.

[a] Based on responses to CIDI-SF, indicative of having experienced a major depressive episode in the previous year.

15-year loss of HALE at age 20 for adults with depression that we report. This may be explained both by real differences in the health experience of the Canadian and US populations and by methodological differences between our studies. Moreover, the hazard ratio for mortality associated with depression we observed (HR = 1.43) is somewhat smaller than the relative risk of mortality of 2.08 for adults with depression reported in the meta-analysis by Walker et al.[16] Studies of older adult populations report a lower life expectancy for participants with depression. Both Chiao et al.[18] and Pérès et al.[20] report life expectancy at 65 years old as lower by approximately one year for participants with depression, whereas Reynolds et al.[19] found that life expectancy at age 70 of individuals with depression in the absence of other chronic diseases was reduced by approximately three years. While these studies found decreases in health expectancy in their participants living with depression, the magnitude of these decreases is less than we found in our study, except for male participants in the Reynolds et al.[19] study. The larger differences may be due to the fact that our measure of HRQOL included attributes not found in the Activities-of-Daily-Living measure of disability used in those three studies.

FIGURE 1
Percentage of life spent in an unhealthy state[a], by sex, age and depression status[b], Canada, 2009/10

Abbreviations: CIDI-SF, Composite International Diagnostic Interview Short Form; HALE, health-adjusted life expectancy; LE, life expectancy; w/o, without.

[a] (LE−HALE)/LE.

[b] Based on responses to CIDI-SF, indicative of having experienced a major depressive episode in the previous year.

We found that a large portion of the lower HALE in participants with depression was due to lower levels in HRQOL. A comparison of each HUI attribute (Table 2) demonstrated that, although there is a clinically meaningful difference between men and women with and without depression for the emotion attribute, there are also meaningful differences for the pain and cognition attributes. Although the association between pain and depression is well documented, the relationship is complex and causal pathways are not thoroughly understood: data support both a model where depression leads to changes in the individual that increase their vulnerability to pain, as well as scenarios where pain symptoms are a risk factor for future depression.[39] Cognitive dysfunction has also been found in a large proportion of patients with depression and has been demonstrated to exist early on in the course of depression; it may even precede diagnosis.[40]

In addition to the expected lower values of HALE associated with lower HRQOL, we also found that a considerable amount of the decrease could be attributed to premature mortality. While our results found women demonstrated the largest losses of life expectancy, other studies on mortality risk and life expectancy according to depression status found that men had the greater mortality risk or loss of life expectancy.[11,17,19,20] However, most of these studies tended to focus on elderly or older adult populations that likely have a different risk profile than the full adult population. Indeed, Shah et al.[41] assessed both sex and age differences in the association of depression with mortality and found significant depression–age–sex interactions: mortality risk increased for men as age increased above 55 years while the inverse was found for women. Further study should be undertaken in non-elderly populations in order to better understand this phenomenon.

Strengths and limitations

Our study benefitted from comprehensive data used to estimate LE and HALE across the age spectrum of adults in Canada. The survey data we used are from large, population-based samples of the Canadian household population: the NPHS allowed us to follow the mortality experience of over 12 000 adult Canadians for 16 years, a longer period than any of the other studies evaluating the association of depression status with life expectancy and/or healthy life expectancy.

Our study has several limitations. When estimating mortality risk, we only considered the first observed episode of probable depression based on the CIDI-SF and did not include depression status at subsequent follow-up. This could have led to misclassification of subjects whose depression status changed.

The definition of depression used in this study (predicted probability of major depressive episode of 0.9) is consistent with the recommended use of the CIDI-SF instrument and corresponds to reporting five to nine symptoms consistent with depression, including one of two cardinal symptoms. This measure was developed for the National Comorbidity Survey in the United States. A 0.9 predicted probability is a high threshold that likely results in more false negatives than false positives, and thus will underestimate, rather than overestimate the burden of depression in Canada.[42]

The CIDI-SF is an optional item in the CCHS and, as such, does not include responses from all Canadian provinces and territories, which may limit the representativeness of our results. We assessed the impact of the missing jurisdictions using an earlier CCHS cycle (2000/01) that included major depressive episode results for all provinces and territories. Age- and sex-specific major depressive episode prevalences from this cycle did not change appreciably when we removed the jurisdictions missing from the 2009/10 cycle, suggesting that representativeness of our study population was not affected by the missing jurisdictions. It should also be pointed out that our measure of depression, recent major depressive episode, does not adequately capture losses in healthy life expectancy specific to longer-term, chronic depression.

The CCHS is a household survey, and by excluding other populations, such as those living in institutions and long-term care facilities, it is possible that the prevalence of depression does not reflect that of the entire Canadian population. There may be differential non-response on the NPHS and CCHS: people with depression may be less likely to respond, resulting in an underestimation of the prevalence of depression. However, this would mean that our estimates are conservative, and that the true burden of depression may be higher than we report.

Our study aimed to describe the association between depression and healthy life expectancy and did not seek to understand the modifying influence of socioeconomic status or of other health conditions. However, in describing the mortality and morbidity of people with depression, it would be inappropriate to adjust for comorbid conditions. The influence on healthy life expectancy of health conditions that are comorbid with depression is unclear. While Pérès et al.[20] only found significant differences in healthy life expectancy between those with and without depression among those reporting three or more chronic conditions, Reynolds et al.[19] found large, significant differences in healthy life expectancy when comparing those with depression to those without in the absence of chronic diseases. Further study is needed to determine the impact of these risk factors and other potentially positive modifying effects, such as social participation, on healthy life expectancy.[18]

Finally, the approach to summarizing population health in this study represents the life and healthy life expectancy experience by a population at a given point in time, based on age- and sex-specific mortality and HRQOL estimates. These period estimates of life expectancy and HALE should only be interpreted as summary measures of population health, and not as the life and healthy life expectancies of any real individual.

Conclusion

This study demonstrates that, at the Canadian population level, women who have recently experienced a major depressive episode have a significantly lower period life expectancy and HALE at age 20 years than those who have not; for men, period HALE at age 20 is significantly lower for those who recently experienced a major depressive episode. Losses in HALE due to lower HRQOL are considerable and, while not as large, losses due to increased mortality risk also contribute to this difference, particularly among women. These findings demonstrate a high burden of depression in the Canadian population.

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Colin Steensma contributed to the study design, developed the first draft of the article, and critically reviewed the article. Lidia Loukine contributed to the study design, conducted all statistical analyses, wrote parts of the article, and critically reviewed the article. Heather Orpana contributed to the study design, wrote parts of the article, and critically reviewed the article. Louise McRae contributed to the study design and critically reviewed the article. Julie Vachon contributed to the study analysis and data interpretation and critically reviewed the article. Frank Mo, Michèle Boileau-Falardeau and Carrie Reid contributed to the data interpretation and critically reviewed the article. Bernard Choi contributed to the study concept and critically reviewed the article.

Data used in this study were accessed through sharing agreements with Statistics Canada and the Canadian provinces and territories. Other researchers can access Statistics Canada data through the Data Liberation Initiative of Statistics Canada.

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EXHIBIT C

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

CHARU DESAI, Plaintiff v. UMASS MEMORIAL MEDICAL CENTER, INC.; UMASS MEMORIAL MEDICAL GROUP; UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, UMASS MEMORIAL MARLBOROUGH HOSPITAL, MAX ROSEN, M.D., DARREN BRENNAN, M.D., STEPHEN TOSI, M.D., AND KARIN DILL, M.D., Defendants.	CIVIL ACTION NO.: **4:19-CV-10520-DHH**

RESPONSES AND OBJECTIONS OF MICHAEL MORRISON, Ph.D., TO DOCUMENT REQUESTS PROPOUNDED BY DEFENDANT UMASS MEMORIAL MEDICAL CENTER INC. IN DOCUMENT SUBPOENA

Pursuant to Rules 26 and 45 of the Federal Rules of Civil Procedure, Michael Morrison, Ph.D. ("Dr. Morrison" or the "Recipient"), hereby responds to the Schedule A attached to the Subpoena to Produce Documents, Information, or Objects ("Subpoena") served on him by Defendant UMass Memorial Medical Center Inc. ("Medical Center"). Recipient made a diligent search of all records and documents in his possession custody, and control. To the extent Recipient is able to obtain possession of documents responsive to Defendant's Requests in the future, these responses will be supplemented accordingly.

The responses set forth below reflect Recipient's present knowledge, information and belief. They may be subject to change or modification based on his further factual investigation or discovery, or on facts or circumstances that may come to his attention during the course of factual investigation. Recipient expressly reserves his right to revise the responses set forth below and/or production made pursuant thereto.

Recipient responds to the specific items in Schedule A of Defendant's Subpoena as follows:

DOCUMENT RESPONSES AND OBJECTIONS

REQUEST NO. 1

All written reports prepared by you or at your direction related to the Expert Review, including any and all drafts, working copies, or versions.

RESPONSE NO. 1

A copy of the Expert Review was already provided to Defendants. Recipient objects to this request to the extent it seeks any additional information, which is protected from disclosure pursuant to Fed. R. Civ. P. 26(b)(4)(B). Subject to and without waiving his objections, recipient has no non-privileged documents in his possession, custody, or control.

REQUEST NO. 2

All notes, summaries, impressions, or opinions related to your analyses performed in the course of the Expert Review.

RESPONSE NO. 2

A copy of the Expert Review was already provided to Defendants. Recipient objects to this request to the extent it seeks any additional information, which is protected from disclosure pursuant to Fed. R. Civ. P. 26(b)(4)(B). Subject to and without waiving his objections, recipient has no non-privileged documents in his possession, custody, or control.

REQUEST NO. 3

All communications between you (and/or any person on your behalf) and Dr. Desai or her attorneys, agents, or any other person on her behalf, related to the Expert Review.

RESPONSE NO. 3

Recipient objects to this request to the extent it seeks information protected from disclosure pursuant to Fed. R. Civ. P. 26(b)(4)(C). Subject to and without waiving his objections, all non-privileged documents in Recipient's possession, custody, or control are produced.

REQUEST NO. 4

All communications between you (and/or any person on your behalf) and any other person regarding Dr. Desai or related to the Expert Review.

RESPONSE NO. 4

Recipient has no such documents in his possession, custody, or control.

REQUEST NO. 5

All documents or information provided to you by Dr. Desai, her attorneys, or her family members on which you based your conclusions or considered in forming your opinions with respect to the Expert Review.

RESPONSE NO. 5

Recipient objects to this request to the extent it seeks information protected from disclosure pursuant to Fed. R. Civ. P. 26(b)(4)(B) & (C). Subject to and without waiving his objections, all non-privileged documents in Recipient's possession, custody, or control are produced.

REQUEST NO. 6

A copy of the Economic Impact Report prepared by you for Tim Kolman, Esq., related to an EEOC complaint, as referenced in your Economic Report.

RESPONSE NO. 6

Recipient objects to this request as not relevant to the subject matter of this action. Subject to and without waiving his objections, responsive documents are produced.

REQUEST NO. 7

A copy of all "refereed sources" and/or academic research you relied on in "establishing" a "reduction in quality of life" and/or which you relied on to determine "suffering multipliers."

RESPONSE NO. 7

Documents in Recipient's possession, custody, or control are produced.

REQUEST NO. 8

All documents you relied upon that set forth a methodology for assigning a dollar value or for calculating a dollar value based on an alleged reduction in quality of life.

RESPONSE NO. 8

Documents in Recipient's possession, custody, or control are produced.

REQUEST NO. 9

All documents establishing an annual value of $4,000 per year for Continuing Medical Education for Dr. Desai.

RESPONSE NO. 9

Documents in Recipient's possession, custody, or control are produced.

REQUEST NO. 10

All documents establishing that UMass Memorial contributed 8% of Dr. Desai's salary annually to her 401k.

RESPONSE NO. 10

Documents in Recipient's possession, custody, or control are produced.

REQUEST NO. 11

All documents evidencing that a younger co-worker was paid $10,000 per year more that [sic] Dr. Desai since 2016.

RESPONSE NO. 11

Documents in Recipient's possession, custody, or control are produced.

REQUEST NO. 12

All documents evidencing that a younger co-worker was receiving "in addition to their regular compensation 1.5 academic/administrative days per week. [Sic]

RESPONSE NO. 12

Documents in Recipient's possession, custody, or control are produced.

Respectfully submitted,
Michael Morrison, Ph.D.,
By his attorneys,

/s/ Patricia A. Washienko
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Dated: August 31, 2021

CERTIFICATE OF SERVICE

I hereby certify that on August 31, 2021, Michael Morrison, Ph.D.'s Responses And Objections To Defendant UMass Memorial Medical Center Inc.'s Subpoena was served by electronic mail only to counsel for the above named Defendants:

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/s/ Patricia A. Washienko
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